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ELECTRO-ENCEPHALOGRAPHY

IV. LOCALIZATION OF SEIZURE WAVES IN EPILEPSY *

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Berger has demonstrated the value of certain electrical signs of brain function which can be obtained from electrodes placed across the head—from forehead to occiput. The electro-encephalogram taken in this manner has been considered for the brain as analogous to the electrocardiogram for the heart. Abnormal brain potentials were found to accompany various pathologic processes which caused gross disturbances in the function of the entire cortex or of regions so located between the electrodes that they made their activity apparent in the composite picture thus obtained. Berger [1] reported a case in which slow waves could be picked up with one electrode directly over a tumor in the central part of the head, even though the electro-encephalogram from the forehead-occiput leads appeared normal. In a case of dementia paralytica in which there were periodic spasms of clonic twitching of the right arm and hand he [2] obtained large seizure waves from bipolar leads over the left precentral region. Fairly normal activity was observed from the right precentral region. Andrews and one of us

* The present report on brain potentials in epilepsy represents a part of a general program of research on brain potentials carried on under a grant from the Rockefeller Foundation to the Emma Pendleton Bradley Home. Additional material has been provided through the cooperation of Dr. Arthur Ruggles, of the Butler Hospital, Dr. Hugh Kiene, of the Charles V. Chapin Hospital, and Dr. Joseph Ladd, of the Exeter School for the Feebleminded, La Fayette, R. I. A preliminary report on some of these results was presented by one of us (Jasper) before the Boston Society of Psychiatry and Neurology in January 1936 (Localized Analyses of the Function of the Human Brain by the Electro-Encephalogram, ARCH. NEUROL. & PSYCHIAT. **36**:1131 [Nov.] 1936).

1. Berger, H.: Ueber das Elektrenkephalogram des Menschen, Arch. f. Psychiat. **94**:16, 1931.

2. Berger, H.: Ueber das Elektrenkephalogram des Menschen, Arch. f. Psychiat. **100**:301, 1933.

(H. H. J.) [3] showed that local seizure waves could be detected from bipolar leads 2 cm. apart on the head over one precentral region which were independent of the electro-encephalograms simultaneously obtained from the contralateral precentral region and the frontal and occipital regions on one side. We maintained that the diagnostic value of the electro-encephalogram would be greatly increased if it were possible to obtain, through the skull, the electrical activity originating from restricted areas of the cortex rather than the complex mass response of the whole brain.

Gibbs, Lennox and Gibbs [4] showed that localizing features of the electro-encephalogram can be obtained in cases of jacksonian epilepsy by the use of an "average" or reference lead on the two ears in relation to a single "active" lead on the head. In less favorable cases it would be difficult to determine whether the differences in records observed from leads across different portions of the head were due to activity somewhere between the two widely separated contacts or to localized discharges in the immediate vicinity of the "active" electrode. With this method of localization Gibbs and his co-workers concluded that "the greatest fluctuations in voltage in petit mal seizures usually appear in the frontal region and that when one part of the brain definitely precedes all others in showing the pathologic activity the frontal lobe is usually the first involved."

In the present paper we shall discuss various methods by which one may determine the region on the head beneath which seizure waves appear to originate in epileptic patients, together with the general differences between seizure waves and pathologic waves obtained from patients with nonepileptic disorders of the brain.

MATERIAL

Our results are based on 117 electro-encephalographic examinations of 55 epileptic patients. Records were taken on some patients eight or nine times during a period of eighteen months. The group was composed of 33 patients with active grand mal, 2 of whom were subject to jacksonian attacks beginning in the right hand; 3 patients with "arrested" grand mal, in 2 of whom the seizures had been of the jacksonian type; 15 patients with active petit mal, and 7 patients who were subject to attacks of a questionable epileptic nature, in 4 of whom the disease proved to be genuine epilepsy. Comparison of these records and those taken under similar conditions on normal subjects is based on 264 examinations of 106 persons, ranging in age from 5 months to 52 years. Comparisons of the electro-encephalograms for epileptic patients and those for nonepileptic patients are based on 200 cases of various neurologic and psychiatric disorders, which are to be reported in detail in a later publication.

3. Jasper, H. H., and Andrews, H. L.: Human Brain Rhythms: I. Recording Techniques and Preliminary Results, J. Gen. Psychol. **14**:98, 1936.

4. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: The Electro-Encephalogram in Diagnosis and Localization of Epileptic Seizures, Arch. Neurol. & Psychiat. **36**:1225 (Dec.) 1936.

TECHNIC

Both bipolar and monopolar records from the right and left frontal, central, parietal and occipital regions of the head were taken according to standard placements of electrodes, as described in a previous report.[5] The amplifiers used for simultaneous recording from four regions of the head were of push-pull design from input to output. No electrode was directly grounded, so that no electrode was common to the ground electrode from other parts of the head. Recording was done with the Westinghouse oscillograph on photographic paper, and the entire amplifier-oscillograph system had a flat frequency characteristic of from 1 to 1,200 cycles per second except when the 100 cycle cut-off filter for reducing disturbance from muscle potentials was used.

Standard light and sound stimuli were introduced during the course of each examination, and definite periods of hyperventilation were produced to induce attacks in epileptic patients, with control experiments on normal subjects undergoing approximately the same amount of hyperpnea.

ARTEFACTS

One of the unavoidable complications of any extensive work with convulsive patients is the recording of electrical disturbances which are not of brain origin, since in most cases some movement occurs with the seizure. Some of these artefacts, such as muscle potentials, are readily distinguished from potentials of brain origin, but others, such as those resulting from movements of the body and eyes, may produce slow potentials in electrodes attached to the head which resemble brain potentials so closely that great care is needed to avoid misinterpretation of records.

We studied the artefacts appearing in records from normal subjects who simulated "3 a second" clonic movements. Simultaneous recording with both monopolar and bipolar leads from two regions of the head were obtained, as shown in figure 1. The movements associated with blinking the eyes were found to produce large, slow waves in the monopolar leads to the frontal region without affecting any of the leads from other regions. A slight effect was occasionally seen from monopolar leads to the precentral region. Movements of the scalp and clenching of the jaw produced chiefly muscle potentials from all leads, with some disturbance in slow potentials from the frontal bipolar leads.

Simulation of the slight clonic body movements seen in some cases of petit mal produces artefacts in all leads which may roughly resemble seizure waves. The clonic movements of the convulsion cannot be simulated precisely, so that it is not to be expected that simulated seizures will produce the same form of artefacts as real convulsive movement. The magnitude and form of the potential artefacts accompanying body movement are sufficiently similar to the disturbances in potential recorded from the surface of the head during a real seizure to lead to distortion of the records from movement artefacts whenever they are taken during extensive clonic movements. We are able to rule out many of these artefacts in our records by signaling every movement of the patient directly on the record as it is taken.

The magnitude of the slow ocular potentials set up across the frontal region of the head is especially serious because of the frequent association of movements ("fluttering") of the eyes with petit mal attacks, even though there may be no

5. Jasper, H. H., and Andrews, H. L.: Electro-Encephalography: III. Normal Differentiation of Occipital and Precentral Regions in Man, Arch. Neurol. & Psychiat. **39**:96-115 (Jan.) 1938.

other motor manifestation of the seizure. These potentials are due to the large corneoretinal resting potential, which has recently been used by Mowrer, Ruch and Miller [6] as a galvanometric method of recording ocular movements. Vertical movements of the eyes may not affect a pair of leads close together on top of the head if they have correct orientation. With monopolar recording when a diffuse lead from the ears is used, this artefact might well lead to the conclusion that the greatest epileptic activity was in the frontal region.

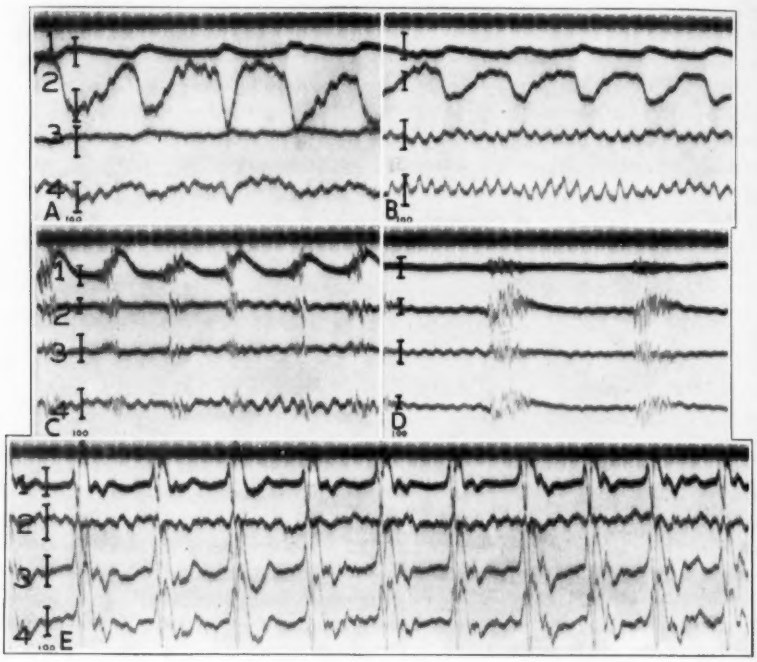

Fig. 1.—Movement artefacts in records for a normal man H. J. *A* was taken during blinking the eyes with (*1*) bipolar and (*2*) monopolar leads to the right frontal region and (*3*) bipolar and (*4*) monopolar leads to the right precentral region; *B*, under the same conditions as those in *A*, except that the two lower records were taken from (*3*) bipolar and (*4*) monopolar leads to the right occipital region; *C*, during movements of the scalp with (*1*) bipolar and (2) monopolar leads to the frontal region and (*3*) bipolar and (*4*) monopolar leads to the precentral region; *D*, during clenching the jaws with the same order of leads as that in *C*, and *E*, during body jerks with the same order of leads as that in *C* and *D*. Calibration lines equal 100 microvolts. Time signal at top indicates 0.1 second.

In order to examine further the disturbances in ocular potentials, electrodes were placed directly across the eye, one at the level of the eyebrow and the other on the skin just below the eye. Records of the disturbances in potentials set up in these electrodes were taken simultaneously with records from electrodes

6. Mowrer, O. H.; Ruch, T. C., and Miller, W. F.: The Corneo-Retinal Eye-Movements, Am. J. Physiol. **114**:423, 1935.

across the head from the ears to the frontal region (8 cm. above the glabella) and to the occipital region (3 cm. above the inion) and from pairs of electrodes on the surface of the head over these regions. Three epileptic patients and 1 normal subject were used. During a petit mal attack in one patient the potentials set up across the eyes were almost identical with those recorded from the ears to the frontal region of the head and were similar and synchronous with potentials observed from both monopolar and bipolar leads to the frontal and occipital regions, as shown in figure 2 *A* and *B*.

The normal subject was able to flutter his eyelids voluntarily with remarkable rapidity and regularity, causing an upward movement of the eyes with each closure of the lids. The potentials recorded across the eyes during the voluntary flutter were smooth, regular waves about 400 microvolts in magnitude and almost identical in form with the potentials from the monopolar frontal leads, which reached only about 120 microvolts. The bipolar leads from the same region as the monopolar lead picked up practically none of these large ocular potentials. Neither bipolar nor monopolar leads over the occipital region were affected (fig. 2 *C* and *D*). This demonstrates that records taken by the so-called monopolar method will include disturbances in potentials set up at a distance between the two leads and that the eyes are an important source of artefacts when such leads are placed from the ears to the frontal region of the head.[7]

LOCALIZATION

In order to obtain a clear picture of the origin and spread of epileptiform discharges from one region to another it is necessary to record simultaneously from three or four regions, with recording technics which insure complete independence of the leads as well as of the multiple amplifier-oscillograph system. With such a recording system and by the use of bipolar leads from 15 to 20 mm. apart, seizure waves can be obtained in one region which do not affect a pair of electrodes placed only 3 or 4 cm. distant on the surface of the head. Precise localization of deep-lying regions is probably impossible by this technic. In our studies localized potentials were obtained from surface aspects of the frontal, precentral, parietal and occipital areas, about 3 or 4 cm. to either side of the midline. Discharges originating subcortically or from underlying distant cortical areas, e. g., the cornu ammonis, might

7. It may be that the potentials recorded across the eyes during the seizure originate in the frontal pole of the brain, as it should be possible to record brain activity with these placements of electrodes. We have attempted to obtain photographic records of the ocular movements during a petit mal attack in the same patient from whom were obtained the potentials shown in figure 2. We made use of the oculophotometer from the Educational Laboratories, Inc., of Brownwood, Texas, which records movements of the corneal high lights on a continuously moving film. After repeated attempts, we obtained legible records during an attack. These records showed rather complex vertical and horizontal clonic movements. When the frequency of the vertical movements could be measured, it appeared to be the same as that of the seizure potentials, although the form of the movement did not seem sufficiently regular to account for the regular potentials recorded across the eyes during a seizure.

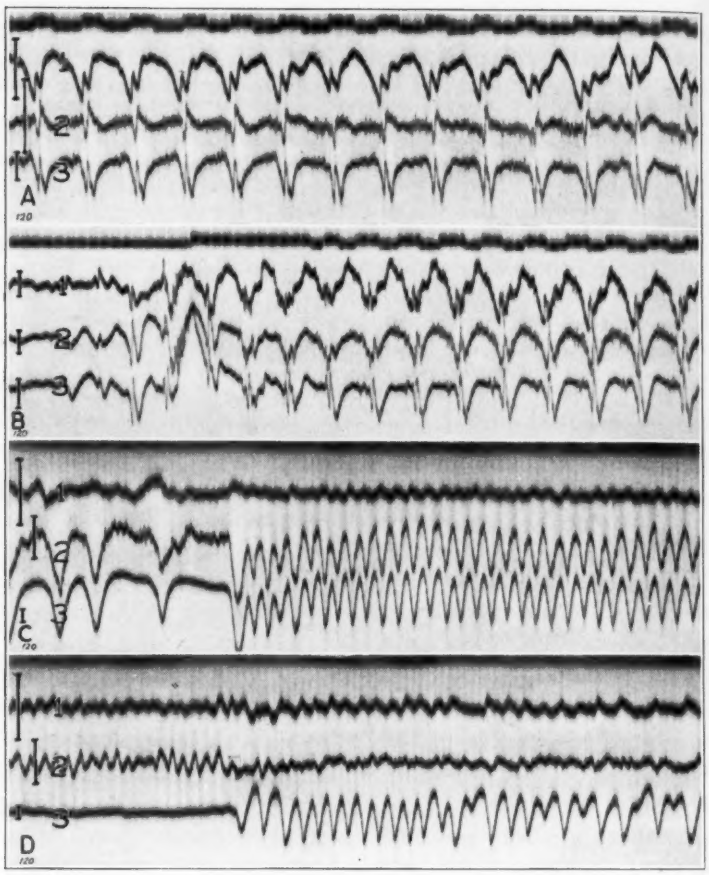

Fig. 2.—Artefacts due to ocular movements in a patient with petit mal during an attack (*A* and *B*) and in a normal subject during voluntary flutter of the eyelids (*C* and *D*).

A. Seizure waves from bipolar leads to (*1*) the left frontal and (*2*) the left occipital region. Record *3* was taken from leads across the left eye (see text).

B. Seizure waves during another attack in the same patient, with monopolar leads to (*1*) the left frontal and (*2*) the left occipital region. The third record was taken from across the eyes, as in *A*.

C. Records from (*1*) bipolar and (*2*) monopolar leads to the frontal region. Record *3* is from leads directly across the eyes.

D. Records taken as in *C*, except that *1* and *2* are from bipolar and monopolar leads to the occipital region. Calibration lines equal 120 microvolts.

Time signal indicates 0.1 second.

spread to the surface and give apparent localizing signs in these areas. One would expect, however, that such attacks might appear simultaneously in the different leads of the electro-encephalogram. In some records seizure waves appeared from the monopolar leads with reference to the ears and not from the bipolar leads on the surface of the head, thus giving an indication, although not the localization, of deep-lying disturbances.

Criteria of Epileptogenic Foci.—1. Precedence of Convulsive Discharges in One Region at the Beginning of an Attack: At the beginning of some petit mal attacks we have recorded from 1 to 5 large potentials occurring at a rate of 3 a second in one region before they spread successively to other regions and developed into visible clinical seizures. An example of such progress of seizure waves in a mild petit mal attack is shown in figure 3. In record *C* the large, slow waves are seen to start in the left occipital region and to arrive at the leads from the left precentral region before reaching the right occipital region. Such an attack as is represented here was associated with no overt movements but with momentary loss of consciousness, or with garbled speech if the patient happened to be talking prior to the attack. More severe attacks in this patient, lasting from ten to fifteen seconds, always originated in a similar manner, spread quickly to involve all regions and were accompanied by slight clonic movements of the eyes and hands. Records taken on this patient on nine occasions between June 1935 and June 1936 showed in all instances the same restricted locus of origin. Similar results have been obtained on other patients, in some of whom the region of onset was the precentral and in others the frontal area. In still other patients the attack appeared either to arrive at all regions simultaneously or to show no consistent precedence in one region.

2. Local Seizure Waves: One of the best signs of an epileptogenic focus is the sporadic discharge of slow waves from restricted areas during periods between clinical attacks. When this local discharge becomes sufficiently great it spreads to other parts of the cortex and results in a more or less generalized seizure, depending on the extent of the spread. This does not happen in some cases; the disturbance remains a "local epilepsy," similar to that described clinically by Holmes,[8] or epilepsia partialis continua. In our experience, the electroencephalogram was the only means of detecting such local seizures in some cases. Figure 3 *A* illustrates the detection of local seizures in the left occipital region, which were not conducted to the bipolar leads from the left precentral and left frontal regions. Record *B* of this figure shows localization in the left occipital region, as compared

8. Holmes: G.: Local Epilepsy, Lancet **1**:957 (May 7) 1927.

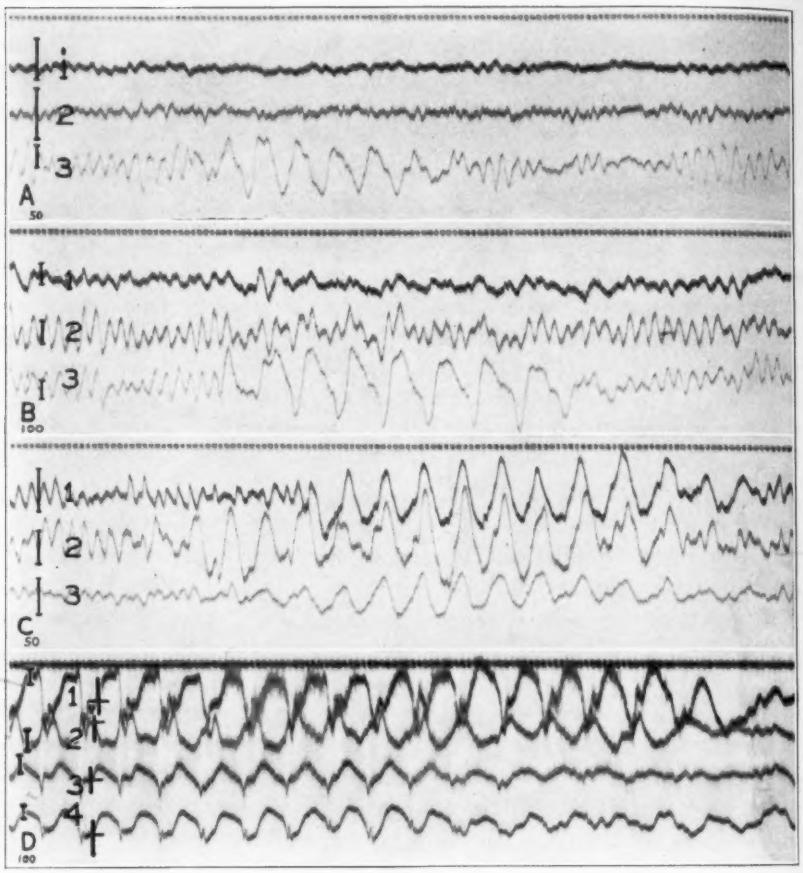

Fig. 3.—Localization of origin and spread of seizure waves in a case of petit mal.

A. Records from bipolar leads to (*1*) the left frontal, (*2*) the left precentral and (*3*) the left occipital region during an abortive attack near the occipital leads. Calibration lines equal 50 microvolts.

B. Records from monopolar leads to (*1*) the left frontal, (*2*) the right occipital and (*3*) the left occipital region. Calibration lines equal 100 microvolts.

C. Records from bipolar leads to (*1*) the right occipital, (*2*) the left occipital and (*3*) the left precentral region. Calibration lines equal 50 microvolts.

D. Records at the end of a typical petit mal attack from bipolar leads to (*1*) the left frontal, (*2*) the left precentral, (*3*) the left parietal and (*4*) the left occipital region. Latencies are indicated by the black crosses at the left of the record. Calibration lines equal 100 microvolts.

Time signal indicates 0.05 second.

with the right occipital and left frontal regions (the potentials being obtained with monopolar leads on these regions in relation to the common diffuse leads on the two ears). Conduction to other regions in a mild attack is shown in *C*, and involvement of all regions in a major attack, with the accompanying increase in amplitude and change in form of the waves, is shown in record *D*.

The persistence of local seizures in the left precentral region in a case in which all clinical convulsions had been arrested for three months by phenobarbital is shown in figure 4. Slight clonic movements of the fingers and hand could be detected occasionally, but there was no loss of consciousness. These waves were not seen to spread to any other part of the brain and could not always be observed from this region. The grand mal attacks had been described as of the jacksonian type, involving chiefly the right side.

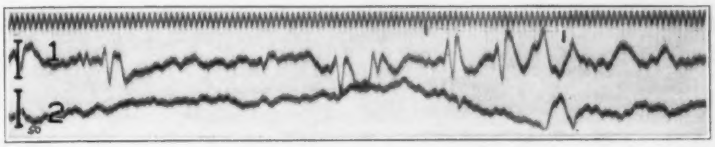

Fig. 4.—Local convulsive discharges in the left precentral region (*1*) which do not appear in the right homologous area (*2*) or from other regions of the head. This patient had shown jacksonian grand mal seizures after an injury to the head. Calibration lines equal 50 microvolts. Time signal indicates 0.04 second.

Figure 5 shows localization in the left precentral focus in another case, in which waves spread readily to the right homologous area, but not regularly to any other of the regions tested. A previous exploratory craniotomy had revealed a few arachnoid adhesions in the left precentral region.

3. Latencies: During a clinical attack there is remarkable synchronization of the discharges from all parts of the brain, the frequency and phase relations of the discharges from different regions being the same at the beginning and at the height of the attack. (This is most readily seen with monopolar leads, since the phase relations may be reversed and the form somewhat more complex with the bipolar leads.) Toward the end of the attack the different regions may get out of step, discharges from one region slowing down and stopping before those from another. There are always, however, small latencies between the discharges from different regions, which make it appear that the disturbance is being conducted from a focus to other parts of the head.

Record *D* of figure 3 illustrates latencies of approximately twenty, thirty-five and sixty milliseconds from the parietal to the occipital, precentral and frontal region, respectively. The results were corrobo-

rated in this patient by records from monopolar leads to these regions. Such latencies may represent not conduction from a parietal focus but merely differences in the time of arrival of the seizure wave at these regions from a distant cortical or subcortical focus. The fact that the same region was located by criteria 1 and 2 favors the interpretation of the latencies on the basis of a cortical focus in the left parietal region.

Figure 5 *B* illustrates latencies of about twelve milliseconds from a focus in the left precentral region to the homologous area on the right side.

Since the precise location of the cortical area beneath the electrodes on the surface of the head is not known and since the lengths of the paths of conduction have not been determined, we cannot determine significant velocities of conduction. Latencies, as criteria of epilepto-

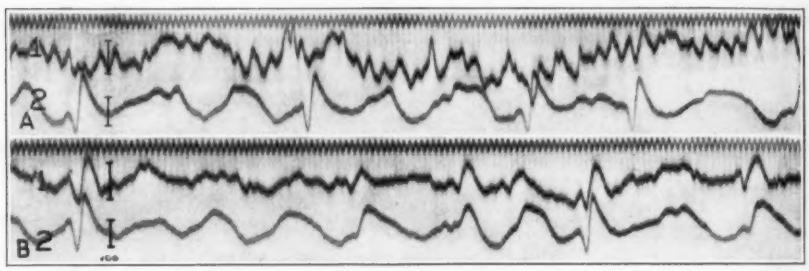

Fig. 5.—Local seizures in the left precentral region (*2*) which spread to the right precentral region (*1*) but not to other regions. This patient had also shown jacksonian grand mal attacks. Calibration lines equal 100 microvolts. Time signal indicates 0.04 second.

genic foci, are significant only at the beginning of an attack, before autonomous seizures have been set up in other regions. They are subject to considerable error, owing to differences in wave form in different regions which make it difficult to know from what portion of the wave to measure the latency. Foci were not determined in our studies by latencies alone. This criterion was used only in addition to those of precedence and local seizures.

4. Relative Potential Magnitudes: The over-all magnitude of seizure waves from bipolar leads in cases of petit mal ranges from 60 to 500 microvolts. Potentials as high as 550 microvolts were recorded from bipolar leads in a grand mal attack, but these may have been spuriously increased by movement artefacts. Monopolar leads give potentials of from 100 to 1,400 microvolts in cases of petit mal, depending on the severity of the attack. The potentials developed during a seizure are therefore from ten to twenty times the magnitude of the spontaneous

activity occurring between attacks. This increase in potential is probably due to an increase in the number of cortical neurons synchronized in each discharge.

The area of onset usually produces the greatest potentials at the beginning of the attack. During the course of the seizure, however, the potentials from this region may become less than those from other regions. Also, in other regions, especially the frontal (as recorded from diffuse ear leads), there may develop potentials of greater absolute magnitude than those produced at any time in the area of onset. In other cases the area of onset produces the largest potentials throughout the attack. Relative magnitudes cannot be used as criteria for locating foci unless they are measured at the onset of the attack.

5. Phase Relations Between Successive Pairs of Electrodes: Adrian and Yamigawa[9] used an ingenious method for determination of the occipital focus of the alpha rhythm from a series of electrodes placed in a line about 1 inch (2.5 cm.) apart on the surface of the head. The phase relations and amplitudes existing between simultaneous records from four successive pairs indicated beneath which electrodes was the largest source of the potential, and changes in phase relations indicated the movement of this focus of activity. More than one focus of maximum activity can also be shown with a sufficient number of simultaneous records (fig. 6).

We attempted to localize regions of origin of convulsive discharges by this method in 6 cases of petit mal, taking records during an attack from four successive pairs of electrodes placed across various parts of the head. The results obtained on patient E. C. are shown in figure 6, in which the phase reversals indicated a point of maximal activity in the parietal region at the beginning of the attack and two foci, one parietal and the other precentral, at the end of the attack. The phase relations are not always clear in records of generalized attacks. This is to be expected, because involvement of a great many areas in simultaneous discharge confuses the record and because waves of activity pass across the cortex. The use of this method with local seizures serves to give more precise indications of the focus and of the direction of conduction than can be obtained from the usual monopolar or bipolar leads to different regions.

6. Triangulation: The principles of localization by this method are the same as those by determination of phase relations in a line of electrodes, except that three electrodes are placed from 15 to 30 mm. apart at the points of an equilateral triangle. After one has detected a local discharge in one of the eight standard placements of bipolar leads

9. Adrian, E. D., and Yamagiwa, K.: The Origin of the Berger Rhythm, Brain **58**:323, 1935.

previously mentioned, the three electrodes are placed on the scalp so as to include this region in the area of the triangle. Three simultaneous records are then taken of the potential differences set up between the points describing the three sides of the triangle. The relative amplitudes and phase relations of the seizure waves appearing in the three records enable one to estimate within a few millimeters a point on the surface of the head beneath which there appears to be a focus and to determine the path of conduction of waves within this area.

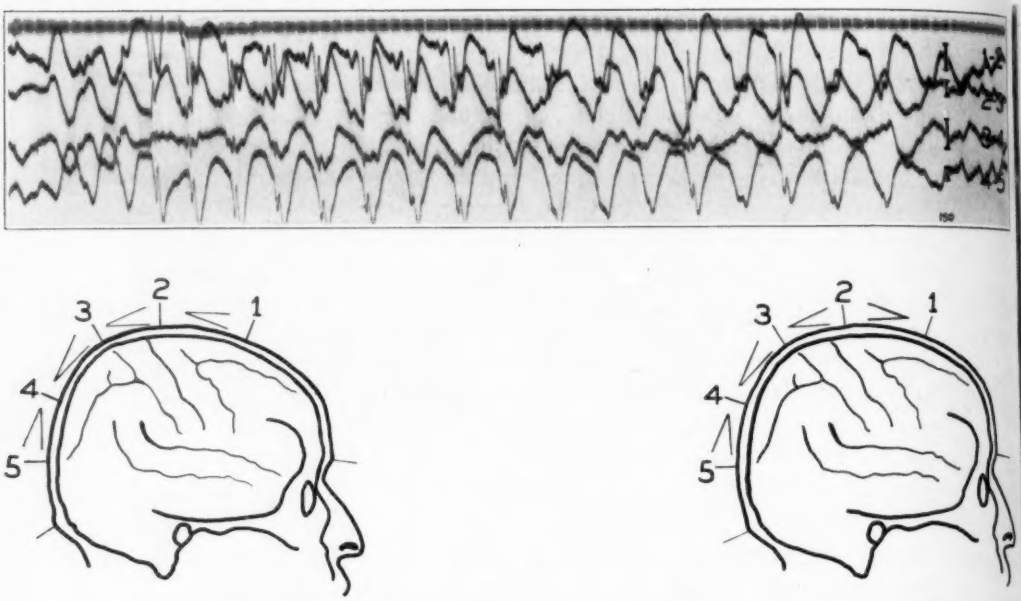

Fig. 6.—Phase reversals throughout a short petit mal attack, showing progressive shift in the focus of maximum activity from the parietal region, in the beginning of the attack, to foci in both the precentral and the parietal region, at the end of the attack. Calibration lines equal 150 microvolts. Time signal indicates 0.1 second.

The use of this method to determine the focus of continued local seizure waves is illustrated in figure 7, in a case of arrested jacksonian attacks formerly beginning in the right hand. The position of the electrodes on the scalp over the left precentral region is represented by the diagram. The base of the triangle was parallel to the midsagittal (dotted) line and just anterior to the midsagittal point (intersection with short vertical line at the left). The distance between the electrodes *A*, *B* and *C* on the head was 2 cm. Lead 2 was placed on the two ears for a monopolar record from lead 1 to electrode *B*, as a check on the triangulation. Leads 3 and 4 were to the second amplifier, leads 5 and 6 to the third amplifier and leads 7 and 8 to the fourth amplifier. An upward deflection on the record indicated that the odd-numbered leads were of negative polarity in relation to

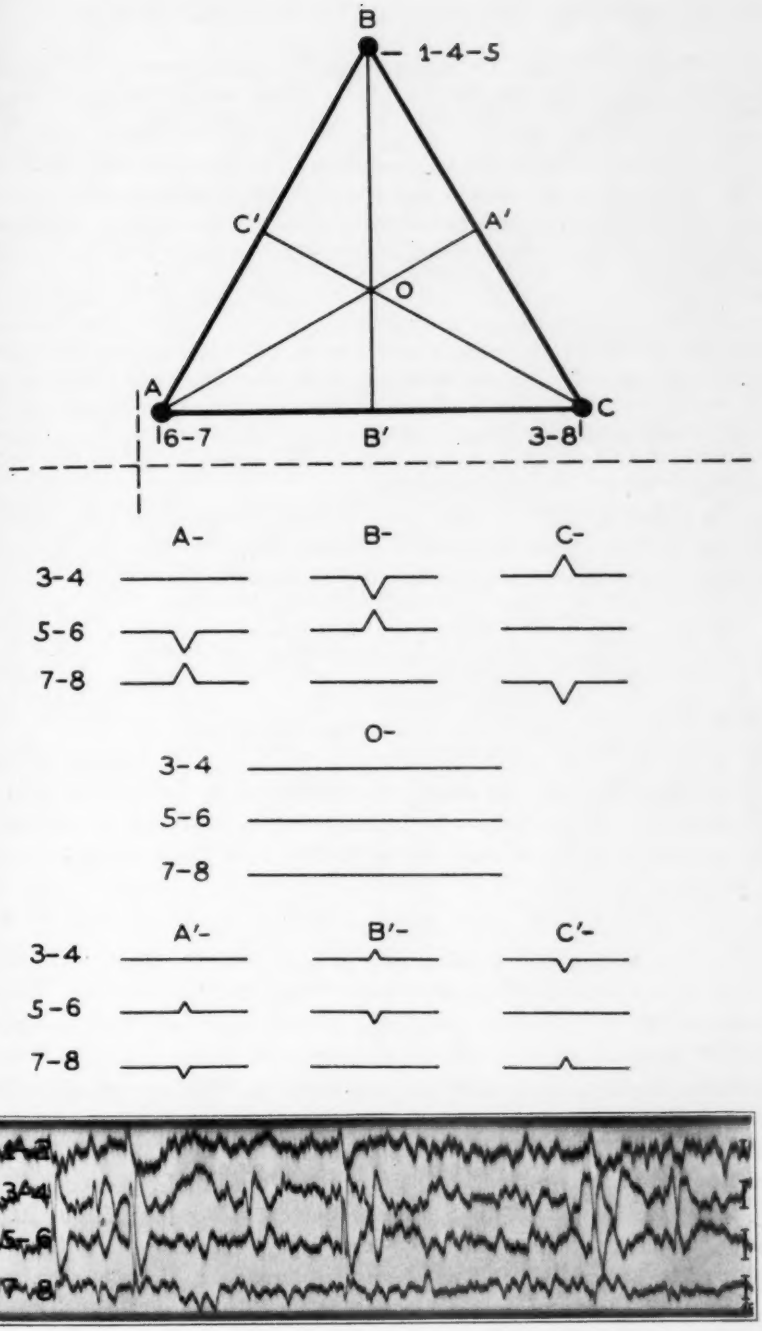

Fig. 7.—Principles of localization by triangulation over a region of local seizures (see text for explanation). Calibration lines in the record equal 50 microvolts.

the even-numbered leads. The key to localization from phase reversals with this set-up is given below the triangle. For example, localization along the line *O-B*, or with electrode *B* negative to the other electrodes, would cause a complete phase reversal of the potentials set up in leads 3 and 4 and 5 and 6, with no difference in potential between leads 6 and 7. This condition is illustrated below the key in an actual record, taken in a case in which the focus was found to be near electrode *B*. Potentials appearing precisely at *O* should set up no difference in potential in any of the leads (except the monopolar). Potentials localized along the line *O-B'*, making *B'* negative to the other leads, should also give phase reversals in leads 3 and 4 and 5 and 6, but the potentials should be smaller and the phase reversals in the direction opposite those appearing when *B* is negative. The phase relations obtaining with negativity at *A* and *A'* and *C* and *C'*, respectively, are also indicated according to the same principles. The form of the convulsive discharge in this record is that of a negative spike followed by a positive after-potential. This is important, since complications in this scheme are sometimes introduced by seizure waves which appear at the cortical surface as positive rather than negative potentials.

Incidence of Anterior and Posterior Localization.—The incidence of localizing signs in our cases according to one or more of the preceding criteria is presented in the following tabulation:

Type of Epilepsy	Frontal-Precentral Localization	Occipital-Parietal Localization	Indeterminate Localization	Total No. of Cases
Grand mal.....	14	6	17	37
Petit mal	5	8	5	18

It is probable that we should have been able to decrease the number of indeterminate localizations in the group of cases of grand mal if it had been possible to study these cases over a longer period.

WAVE FORM

Seizure waves vary considerably in form with the type and severity of the attack and with the region from which they are obtained. Simultaneous records from four parts of the head, with both monopolar and bipolar leads, failed to yield any characteristic forms for specific brain regions, the variation in one region being as great as the differences between regions.

There are two distinct components of seizure waves. The "spikes" [10] vary in duration from thirty to fifty milliseconds and may occur singly or in groups of from 2 to 5 waves repeated at a rate of about 20 per second, each group occurring at about 3 per second. After the spike, or usually before the end of the spike activity, a slow smooth wave appears, which lasts from two hundred to two hundred and fifty milli-

10. We do not imply any relation between these "spikes" and the spike of the action potential in the peripheral axon.

seconds. The magnitudes of the two components appear to vary independently one of the other, so that the spike may appear with little or no evidence of a slow potential. The slow wave may appear also with no spike activity, although both components usually appear together in a definite pattern at some time during the course of a severe generalized petit mal attack. They may occur together also in sporadic local seizures without a clinical attack. The spike occasionally may be of greater absolute magnitude than the slow wave, but usually during the course of the attack the slow wave is equal to or two or three times greater than the spike. The spike may drop out toward the end of the attack, leaving only the slow wave, or the slow wave may (rarely) drop out, leaving the spike.

The polarity of brain potentials is difficult to determine, since their observed polarity may not be that of the potential at the source of activity. Bartley and Bishop [11] observed positive surface potentials, which they assumed to represent negativity beneath the surface of the cortex. The difficulty is greatly enhanced in records taken through the unopened skull. Our best records of seizure waves which appeared to be of cortical origin, however, usually indicated that the major portions of both the spike and the slow wave are negative waves at the top of the head, there being often a slight positive component at the end of the slow wave. This is corroborated by our records taken directly from the surface of the cortex in the cat after the local application of strychnine. Before the strychnine had reached the deep-lying areas, the convulsive spikes were negative at the cortex in relation to a diffuse electrode on the skull. The first aspect of the slow after-potentials is also usually negative at the surface of the cortex, although there may be a late positive component. There are a few notable exceptions in which the major after-potential appears to be positive, e. g., that recorded with the monopolar lead in figure 7.

The spike and after-potential formation occurring in many cases of petit mal and in seizures resulting from the local application of strychnine to the cortex of the cat suggests a striking analogy to the effect of drugs and tetanization on the isolated nerve described by Gasser [12] and his associates. Experiments now in progress in our

11. Bartley, S. H., and Bishop, G. H.: Factors Determining the Form of the Electrical Response from the Optic Cortex of the Rabbit, Am. J. Physiol. **103**: 173, 1933.

12. Gasser, H. S.: Changes in Nerve-Potentials Produced by Rapidly Repeated Stimuli and Their Relation to the Responsiveness of Nerve to Stimulation, Am. J. Physiol. **111**:35, 1935. Graham, H. T., and Gasser, H. S.: Augmentation of the Positive After-Potential of Nerves by Yohimbine, Proc. Soc. Exper. Biol. & Med. **32**:553, 1934.

laboratories serve to make more precise the close similarity between the electrical properties of peripheral axons and those of cortical neurons.

The convulsive discharges in grand mal attacks, so far as they can be observed free from movement artefacts, appear to have a somewhat different form, characterized by bursts of large spikes with relatively small after-potentials. This is probably a variation of the same type of activity.

We agree with the conclusions of Gibbs, Lennox and Gibbs [4] that the form of the seizure waves in petit mal epilepsy is characteristic for epileptic discharges. We have not observed such characteristic sequences of potentials in our examinations of patients with many types of nonepileptic disorders unless some clinical sign suggested at least a borderline epileptic condition, even though this condition was not always noticed until the seizure waves were observed in the electroencephalogram.

There are wide individual variations in the form of seizure waves, some of which may be referable to certain neuropathologic conditions. Sporadic spikes and slow waves, occurring sometimes together and sometimes independently in a particular form, as shown in figures 4, 5 and 7, have been found only over regions of the cortex in which there was a traumatic scar, as shown by exploratory craniotomy (2 cases). One patient presented short bursts of from 3 to 10 smooth, slow waves at a frequency of 3 per second which broke suddenly into what was otherwise a normal alpha rhythm from the occipital region. These occurred more frequently in the left occipital region but occasionally spread to other areas. Autopsy in this case showed diffuse marginal gliosis of the cortex, most marked in the left occipital lobe. Forms of seizure waves observed in the cases of porencephaly, lead encephalopathy and carbon monoxide poisoning in which the pneumo-encephalogram had shown gross damage of the cortex beneath the regions from which the wave forms were obtained differed greatly from those in the cases in which the pneumo-encephalogram was normal. Seizure waves from grossly pathologic tissue appear to differ from those obtained from relatively normal tissue. Further correlations of electroencephalographic results with autopsy observations might show important relationships between brain potential patterns and specific pathologic conditions.

CONCLUSIONS

Methods of localizing the region of the head beneath which seizure waves appear to originate have been presented, based on the results of 117 electro-encephalographic examinations of 55 epileptic patients. Six criteria for epileptogenic foci were found useful in localization from

electrodes placed on the surface of the scalp: (1) precedence of seizure waves in one region at the beginning of an attack, (2) appearance of local seizure waves from one region only during the intervals between generalized attacks, (3) latencies between discharges recorded simultaneously from different regions of the head at the beginning of an attack, (4) relative magnitudes of seizure waves from different areas, (5) phase relations between successive pairs of electrodes and (6) triangulation over the region of a local seizure. Localizing signs suggesting primary involvement of the anterior portion of the head were obtained in 14 of 37 cases of grand mal and in 5 of 18 cases of petit mal. The posterior region of the head appeared to be primarily involved in 6 of 37 cases of grand mal and in 8 of 18 cases of petit mal. Localizing signs were obtained in 33 of the 55 patients examined.

Wide variations in form were observed, with some indications that specific forms may be symptomatic of the neuropathologic condition forming the basis of the seizures, the wave forms from over traumatic scars being specific perhaps to this condition and the seizure waves from grossly damaged cortical tissue also being different from those arising on a different pathologic basis.

The "spiked" portion of the seizure wave appears to vary independently of the slow wave portion, indicating that they may be related, but separate, aspects of the epileptic discharge.

Characteristic seizure waves were found only in patients with epilepsy or with some borderline epileptoid condition, and not in 200 patients with clearly nonepileptic disorders.

DIFFERENTIAL FEATURES OF "CEREBELLAR" AND "VESTIBULAR" PHENOMENA IN MACACUS RHESUS

PRELIMINARY REPORT BASED ON EXPERIMENTS ON THREE HUNDRED MONKEYS

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Much of the early work on cerebellar and vestibular function involved large experimental lesions, for example: complete removal of the cerebellum, hemidecerebellation or large puncture lesions of the lateral lobes or vermis. Such large lesions, even if the ever present possibility of complicating lesions was disregarded, always raised the question of the simplicity of the symptomatic elements. The same may be said of human clinical material. Because of the probability of existence of side-effects in much of the experimental work, and certainly in most of the human clinical material, and because of the generally admitted close relationship of the cerebellum and the vestibular system, it seemed worth while to investigate the differential features of lesions of the cerebellar and the vestibular system and the functional interrelationships of the two systems. This was made possible by the large number of experimental animals in our series with anatomically controlled lesions of the various structures within the posterior fossa.

The major aspects of cerebellar and vestibular anatomic relations are well known. One need only consult a recent textbook on neurology, such as that by Tilney and Riley [1] or Ranson,[2] to note the following facts with regard to the cerebellum:

1. It is connected on the afferent side by several tracts with certain nonvestibular structures. These include the spinal cells of origin of the

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1. Tilney, F., and Riley, H. A.: The Form and Function of the Central Nervous System, New York, Paul B. Hoeber, 1923.

2. Ranson, S. W.: The Anatomy of the Nervous System from the Standpoint of Development and Function, Philadelphia, W. B. Saunders Company, 1935.

dorsal and ventral spinocerebellar tracts, the inferior olive, the nucleus lateralis medullae, the external cuneate nucleus and the pontile nuclei.

2. On the afferent side, involving primarily the inferior and middle cerebellar penduncles, little mention is usually made of vestibular relationships, despite the early claims made by Cajal [3] and repeated by Jones [4] and others. As a result of recent experimental work on cerebellar function, little has been found physiologically to support any concept of vestibular participation in the structures mentioned.

3. On the efferent side, involving particularly the superior cerebellar peduncle, it would be more difficult to state whether, as a result of intracerebellar admixture of vestibular and cerebellar influences, participation of the vestibular apparatus may not manifest itself through the action of this peduncle. Indeed, Winkler [5] claimed direct vestibular participation in the superior cerebellar peduncle, especially near the region where it enters the brain stem.

As can be seen from the brief enumeration, the connections mentioned involve primarily those of nonvestibular origin. There is, however, still another region of the cerebellum in which it seems that a much closer relationship of vestibular and cerebellar influences must occur. This region includes the central portion of the cerebellum, including the roof nuclei and the periventricular fibers, which apparently place these nuclei in relation with medullary and periventricular vestibular nuclei. Despite the fact that many investigators have not confirmed, and, in fact, Lorente de Nó [6] has denied, the early claims of Cajal [3] of a direct projection of the vestibular nerve in the cerebellum, it is generally admitted that the periventricular, usually known as the juxtarestiform, fibers connect the vestibular nuclear complex with the cerebellar roof nuclei. The relationships within this fiber system are usually said to be bidirectional, thus presenting vestibulocerebellar and cerebellovestibular connections. It is not necessary here to discuss at length the extent, composition and relationships of this region, including those of the so-called hook bundle of Russell. These may well be studied from the works of Cajal,[3] Winkler,[7] Leidler,[8] Van Gehuchten,[9] Lorente de Nó,[6] Fuse [10] and Bender.[11] It suffices to show that in the periventricular

3. Ramón y Cajal, S.: Beitrag zum Studien der Medulla oblongata, des Kleinhirns, und des Ursprungs der Gehirnnerven, Leipzig, J. A. Barth, 1896.

4. Jones, I. H.: Equilibrium and Vertigo, Philadelphia, J. B. Lippincott Co., 1918.

5. Winkler, C.: Manuel de neurologie, Haarlem, de Erven F. Bohn, 1927, vol. 1, pt. 3, p. 342.

6. Lorente de Nó, R.: Anatomy of the Eighth Nerve: The Central Projection of the Nerve Endings of the Internal Ear, Laryngoscope **43**:1 (Jan.) 1933.

7. Winkler,[5] 1921, vol. 1, pt. 2.

(Footnotes continued on next page)

region there exist anatomic possibilities of cerebellar and vestibular interaction.

In speaking of the "cerebellar" and "vestibular" systems, we shall restrict ourselves to a consideration of the relationship of fibers known to be connected primarily with one or the other of these systems. In the "vestibular" group of lesions we shall include lesions of such structures as the labyrinth, the vestibular nerve, the various central vestibular nuclei and the posterior longitudinal bundle. In the "cerebellar" group of lesions we shall include those of various cortical regions of the cerebellum, the dentate nuclei and the superior, middle and inferior cerebellar peduncles. In speaking of lesions of the roof nuclei or the juxtarestiform system, we shall, in reality, be speaking of combined vestibulocerebellar or cerebellovestibular lesions. The same is true in a sense in speaking of total removal of the cerebellum. The accompanying diagram illustrates the main lesions discussed in this paper. As can be seen, three types of structures, and hence of lesions, are considered.

1. Structures which are, on the basis of their anatomic connections, primarily cerebellar. These regions are represented by the areas shaded with crosses.

2. Structures which are, on the basis of their anatomic connections, primarily vestibular. These structures are shaded with lines.

3. Structures primarily of the deeper portions of the vermis and the periventricular fiber systems which may, on the basis of their anatomic connections, be considered as vestibular or cerebellar or, better, as vestibulocerebellar or cerebellovestibular. This region is stippled.

It seemed to us of importance to analyze carefully the so-called cerebellar and vestibular elements in the symptom complex associated with various lesions of the two systems because it seemed that, in the light of some of our recent experimental work on the cerebellum, failure to specify adequately the exact site of the lesion has often introduced unjustified conclusions as to the functional activity of certain parts. This was particularly noticeable in much of the early work on the cerebellum, in which features that appear now to have been due to vestibular complications were ascribed to lesions of the cerebellar

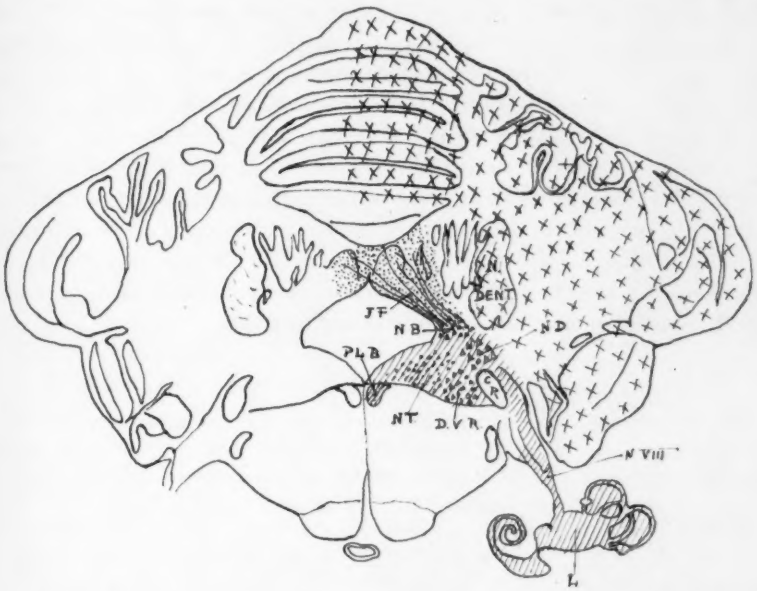
8. Leidler, R.: Experimentelle Untersuchungen über das Endigungsgebiet des Nervus vestibularis, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **20**:256, 1912-1913; **21**:151, 1914.

9. Van Gehuchten, A.: Le faisceau en crochet de Russell ou faisceau cérébello-bulbaire, Névraxe **7**:117, 1905.

10. Fuse, G.: Die innere Abteilung des Kleinhirnstiels, Arb. a. d. hirnanat. Inst. in Zurich **6**:29, 1912.

11. Bender, L.: Corticofugal and Association Fibers Arising from the Cortex of the Vermis of the Cerebellum, Arch. Neurol. & Psychiat. **28**:1 (July) 1932.

apparatus and were used as the basis for theories of cerebellar function. Indeed, the use of many elements which were undoubtedly complex but were assumed to be relatively simple probably led to the divergent theories of cerebellar function. According to one view, the cerebellum plays a definite role in equilibrium. This view is embodied even in the relatively recent work of Ingvar.[12] According to the other view, ably formulated by Luciani [13] and now more generally accepted, the cerebellum exerts a coordinating influence on muscular movements. This has been confirmed experimentally by Tilney and Pike.[14] The strongest evidence against the theory that the cerebellum is an organ of "equilibrium" was advanced by the fundamental work of Magnus and his



In this diagram, *L* indicates the labyrinth; *N VIII,* the trunk of the eighth nerve; *CR,* the corpus restiforme; *ND,* Deiters' nucleus; *NB,* Bechterew's nucleus; *NT,* nucleus triangularis; *DVR,* the descending vestibular root and nucleus; *JF,* juxtarestiform fibers; *PLB,* the posterior longitudinal bundle; *N DENT,* the dentate nucleus, and *N FAST,* the nuclei fastigii.

The areas shaded with lines represent vestibular structures; those shaded with dots, cerebellovestibular structures, and those shaded with crosses, pure cerebellar structures.

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12. Ingvar, S.: Zur Phylo- und Ontogenese des Kleinhirns, Folia neuro-biol. **11**:205, 1918.

13. Luciani, L.: Il cervelletto, Florence, successori Le Monnier, 1891.

14. Tilney, F., and Pike, F. H.: Muscular Coordination Experimentally Studied in Its Relation to the Cerebellum, Arch. Neurol. & Psychiat. **13**:289 (March) 1925.

co-workers,[15] which indicated that all the position or labyrinthine reflexes so important in equilibrium may be normally retained even after complete ablation of the cerebellum.

During the past five years or more, operations have been performed in our laboratory on over 300 Macacus rhesus monkeys. For the most part, these concerned lesions of various parts of the somatic sensory system in the posterior fossa, lesions of the various cerebellar peduncles, ablations of the whole or various portions of the cerebellum and lesions of all the well known parts of the vestibular apparatus, including the pathways of connection with the cerebellum. Since a clinical study has been made of all these animals and, particularly, since serial sections of the brains have presented a clear picture of the anatomic structures involved in the lesions, a tentative summary may be made at this time of the symptoms which have been found to be uniformly associated with lesions of various parts of the vestibular system, and these symptoms may be compared with those produced by all the better known lesions of the cerebellum. This seems desirable because even at present one may experience considerable difficulty in delimiting clinically vestibular and cerebellar elements in the syndromes commonly associated with pathologic changes in the posterior fossa. Our purpose is to present merely the facts as we have seen them in the clinical pictures of this large series of monkeys. We shall not attempt at this time to formulate any theories as to cerebellar or vestibular function.

MATERIAL AND METHODS

The experiments were all performed on Macacus rhesus monkeys averaging from 8 to 10 pounds (3.6 to 4.5 Kg.). All the lesions were produced with specially constructed knives or hooks. Ether anesthesia was used throughout. Many of the procedures have been described in previous papers, and it will be unnecessary to mention them in detail here. In general, a simple posterior occipital approach was made to the cerebellum, and the posterior inferior surface of the cerebellum was exposed. An approach to the structures of the floor of the fourth ventricle was made by simple upward retraction of the cerebellum. In all cases the animals were observed clinically in the acute stage and at various intervals up to the time of death, which varied from eleven days, for Marchi preparations, to two years. Moving pictures were taken to demonstrate the more typical findings. After the animals were killed, serial sections of each brain were prepared and stained by the Marchi, Weigert or Nissl methods. In all cases it was thus possible to reconstruct the lesion as it actually existed in the specimen rather than as it theoretically existed in the mind of the experimenter.

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15. (*a*) Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924. (*b*) Magnus, R., and de Kleyn, A.: Experimentelle Physiologie des Vestibularapparates bei Säugetieren mit Ausschluss des Menschen, in Alexander, G., and Marburg, I.: Handbuch der Neurologie des Ohres, Berlin, Urban & Schwarzenberg, 1923, vol. 1, p. 465; Körperstellung Gleichgewicht und Bewegung bei Säugern, in Bethe, A., and others: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1930, vol. 15, no. 1, p. 29.

Table 1 summarizes the lesions to be considered at this time. They have been divided into three groups: The first contains all lesions of the structures investigated which are generally admitted to be in direct relationship with the vestibular system and are thus classified here as "vestibular"; the second, all lesions of the structures unquestionably related to cerebellar function, and the third, the few lesions of the periventricular structures which are apparently birelational in the sense that they comprise vestibular and cerebellar anatomic relationships.

OBSERVATIONS

At this point it is necessary to repeat that we are not reporting all the individual observations associated with each lesion, whether of cerebellar or of vestibular structures. We have abstracted from the mass of material available what we consider to be the typical features of cerebellar or vestibular lesions without regard to specific instances in which great variations in intensity, as well as in direction, of the mani-

TABLE 1.—*Summary of Sites of Lesions Produced in This Study*

Cerebellar Lesions	Vestibular Lesions	Combined Cerebellovestibular Lesions
1. Dorsal spinocerebellar tract	1. Labyrinth	1. Juxtarestiform fibers
2. Ventral spinocerebellar tract	2. Eighth nerve trunk	2. Cerebellar roof nuclei
3. Restiform body (various levels)	3. Descending vestibular nucleus	3. Superior cerebellar peduncle (questionable)
4. Various cortical regions of lateral lobe, e. g., crura 1 and 2, and lobus paramedianus; cortex of vermis	4. Deiters' nucleus	4. Total decerebellation
5. Dentate nucleus	5. Nucleus triangularis	5. Hemicerebellation
6. Middle cerebellar peduncle	6. Bechterew's nucleus	6. Accidentally involved "cerebellar" structures, e. g., restiform body plus vestibular nucleus
7. Superior cerebellar peduncle (majority of cases)	7. Posterior longitudinal bundle	
	8. Combinations of lesions in 3, 4, 5 and 6	

festations may occur. For instance, in speaking of lesions of the vestibular apparatus, we are concerned at this time not with whether spontaneous nystagmus is vertical or toward or away from the side of the lesion but with the fact that spontaneous nystagmus occurs as a more or less constant feature of vestibular lesions. Likewise, we are concerned not with the question of exact bodily localization of the functional manifestations of lesions of the cerebellum but with the type of manifestation, such as muscular incoordination. Thus, in considering a lesion of crus 1 or crus 2 of the lateral lobe, we are concerned not with the question whether the manifestations were confined to the forelimb or the hindlimb but with the fact that ataxia, or perhaps a certain dissociation of movement or lack of smoothness in movement, best described by the term "asynergia," does or does not exist with such pure cerebellar lesions.

Vestibular Dysfunction.—With these points in mind, it is possible now to proceed to a consideration of the symptoms as detected in typical cases. The prototype for vestibular dysfunction in the monkey may per-

haps best be observed in cases of peripheral lesions of the vestibular apparatus, namely, labyrinthectomy or section of the vestibular nerve. Animals with these lesions present all the typical symptoms, except incoordination of movements of the eyes, which can be attributed to certain central lesions of the vestibular apparatus.

Table 2 presents a summary of what we believe to be typical findings in monkeys with vestibular dysfunction. As can be seen from the table, postural asymmetries are the rule. The magnitude and direction of the asymmetries depend on the particular animal investigated, as well as on the structure of the vestibular complex involved in the

TABLE 2.—*Effects of Purely Vestibular Lesions in Monkeys* *

A.	Abnormalities affecting the body as a whole or unit
I.	Posture: Asymmetries the rule
	Head: Usually shows torsion of chin to one side
	Limbs: Usually show difference between the two sides, e. g., flexion on one side and extension on the other
	Trunk: May show bending toward one side
II.	Movements in contact with solid objects
	Walking: May fall, deviate or circle to one side
	Climbing: May deviate laterally on climbing wire screen; may spiral on climbing straight bar
III.	Movements in relatively homogeneous mediums
	Air: Disorientation as expressed by deviation or spiraling around one or more axes on jumping the rule
	Water: Disorientation as expressed by spiraling or random movement the rule with animal under surface
B.	Movements of parts (limbs, etc.)
I.	Movements referable to parts other than head
	Usually good coordination if body is stabilized as a whole; no definite ataxia or dysmetria
II.	Movements of eyes
	Spontaneous nystagmus: Usual in early stages
	Induced nystagmus: Some abnormalities the rule
	Coordination: May be deficient with lesions of posterior longitudinal bundle
III.	Muscular tonus: Inconstant changes; in direction of hypotonia with small unilateral lesions in early stages
IV.	Tendon reflexes: Inconstant changes; in direction of hyporeflexia with unilateral lesions in early stages
V.	Special reflexes: Abnormalities of various labyrinthine or postural responses the rule

* Disabilities tend to be severe and long lasting, particularly in cases of bilateral lesions. Typical unilateral symptoms are produced by a central lesion even after bilateral degeneration of the labyrinth or the eighth nerve.

lesion. Postural asymmetries, involving usually the head or the limbs or both, are found as a rule in cases of vestibular lesions, especially in the acute stages following operation. As a rule, they persist at varying degrees in the chronic stages.

The second feature, practically always associated to some degree with vestibular lesions, is disturbance of movement of the body as a whole (asymmetries of movement). All the animals with vestibular dysfunction showed a tendency either to fall in a certain direction or to roll to one side around a longitudinal axis. Generally, the tendency toward asymmetries of movement of the entire body around any arbitrarily chosen axis is associated with abnormalities in the posture of the head. Whether or not this is a causal relationship is not clear.

The asymmetries in movement of the body as a whole with relation to such an arbitrarily chosen axis are manifested particularly in movements in a relatively homogeneous medium, such as air or water. They are best studied by allowing the animal to jump freely into space; to jump forward and upward toward a cage; to fall freely from an abnormal position, such as the back-down position or to swim under water, so as to eliminate to a great extent compensatory influences due to vision. An animal with a vestibular lesion as a rule shows these asymmetries and deficiencies in motion through relatively homogeneous mediums to a considerable extent, especially before any relearning has occurred after the operation. For example, a monkey after labyrinthectomy, section of the vestibular nerve or lesion of the vestibular nuclei may show marked disability in jumping in a situation in which a normal monkey could easily carry out the act successfully. Disability due to rotation of the body around the long axis while the animal is in the air may be so marked as to result in severe falls in the early stages of the experiment. In the chronic stages it is difficult to make such an animal jump. It has apparently learned that the disability has disagreeable consequences. However, if the monkey is forced to jump, the disability is brought out to a greater or less degree, depending on the particular lesion in the case. Some of these disabilities, such as the inability of the animal with a large vestibular lesion to swim under water, may be permanent. An animal with both labyrinths removed is practically sure to drown if the head is placed under water, even many months after the operation. The animal with one labyrinth removed may in the early stage show definite spiraling movements to one side when the head is placed under water. These may result in drowning if the animal is not removed from the tank. However, after several disagreeable experiences the unilaterally labyrinthectomized monkey may learn to keep its head above water and to resist violently any attempts of the examiner to submerge it.

A third feature of the vestibular phenomena is represented by various combinations of abnormal movements of the eyes, including spontaneous nystagmus, disturbance in induced nystagmus and incoordination of ocular movements. Incoordinated movements of the eyes were found in our cases only when the structures involved were near the midline and included particularly the posterior longitudinal bundle. Incoordination of ocular movements was not found in association with any peripheral lesion or unilateral lesion of one of the primary vestibular centers. Spontaneous nystagmus, a characteristic of the early stages of practically all the vestibular lesions, must not be confused with nystagmus in the direction of gaze, which is elicited by having the animal look in a particular direction. The spontaneous nystagmus referred to in this paper is nystagmus with the eyes in the resting position.

The direction of the nystagmus is denominated by the direction of the quick component. In all cases in which spontaneous nystagmus occurred in a particular direction, involvement of a particular predominantly vestibular structure could always be seen. The abnormalities in induced nystagmus vary, depending on the method used to elicit the nystagmus, the particular lesion in the case and the time allowed to elapse after the operation before the tests were made. In this paper we cannot discuss the particular variations in all cases. These will be reported at length elsewhere. However, we may say that spontaneous nystagmus and variations in induced nystagmus, including incoordination of ocular movements, were found only in cases in which vestibular structures of certain types were involved in the lesion.

Abnormalities in muscular tonus and in the usual tendon reflexes, which may accompany vestibular lesions, were difficult to ascertain accurately. No method of measuring muscular tonus sufficiently precise to justify any important conclusion was at hand. It seemed, however, that considerable variations in tonus, in general on the side of hypotonia, were detectable in some monkeys with vestibular lesions, particularly when the lesion involved a large amount of the primary vestibular nuclei, the labyrinth or the vestibular nerve.

Abnormalities in movements of portions of the body with reference to other portions—for example, movement of the hand or forearm with reference to the upper part of the arm—were not present in animals with vestibular lesions. The animals showed nothing which we could call ataxia or dysmetria in the sense in which these terms are applied to cerebellar dysfunction. In cases in which the animal with a vestibular lesion frequently missed objects for which it was reaching, it was usually found that missing the object was the effect of an abnormal posture or movement of some other portion of the body rather than of actual dyssynergia of the parts investigated. For instance, a monkey with a vestibular lesion was seen to miss an article of food which was offered it. It was usually found that the animal ceased missing food when the trunk or the head was held in the normal, stationary position. This, of course, was not observed in animals with cerebellar lesions, in which the dyssynergia, if present, persisted in spite of the immobility and symmetrical posture of the head and trunk.

All the animals with vestibular lesions, particularly when the lesion involved the primary nuclei, vestibular nerve or labyrinth, especially in the acute stages following experimentation, showed some abnormality of the special reflexes usually ascribed to the vestibular system. These abnormalities involved the various position reflexes and the labyrinthine reflexes, which were studied at length by Magnus,[15a] Magnus and de

Kleyn,[15b] Rademaker [16] and others. These abnormal findings are to be compared with the retention of all normal vestibular reflexes in animals with cerebellar lesions, even those with complete removal of the cerebellum.

With regard to the intensity of the disability: Animals with widespread vestibular lesions (bilateral labyrinthectomy, section of the eighth nerve or large bilateral lesions of the vestibular nuclei) showed marked disability in the acute stage of the experiment. This disability persisted for a long time, and the essential features of apparent spatial disorientation or lack of orientation of the body as a whole with reference to an arbitrarily chosen axis in relatively homogeneous mediums persisted indefinitely. However, "compensation" or a degree of participa-

TABLE 3.—*Effects of Purely Cerebellar Lesions in Monkeys* *

I. Posture:	Definite asymmetries rare
	Head: Usually normal
	Limbs: Usually symmetrical and normal
	Trunk: Usually normal
II. Movements in contact with solid objects	
Walking, Climbing	Falling, deviation and instability may occur, but apparently are related to musclar incoordination
III. Movements in relatively homogeneous mediums	
Air, Water	Within normal limits
IV. Movements of parts of body (limbs, etc.) with reference to other parts:	Incoordination of varying degrees usual; ataxia or dysmetria
V. Movements of eyes	
	Spontaneous nystagmus: Usually not present
	Induced nystagmus: Usually normal except for possibly prolonged responses
	Coordination: Usually normal
VI. Muscular tonus:	Inconstant changes; in direction of hypotonia with unilateral lesions in early stages; large removals followed by rapid exhaustibility (asthenia?)
VII. Tendon reflexes:	Inconstant changes; in direction of hyporeflexia with unilateral lesions in early stages
VIII. Special reflexes:	Usually within normal limits

* In the reactions indicated in sections I, II and III, the body is generally well oriented as a whole or a unit.

tion of other structures in response to the stimulation of a central vestibular mechanism could be seen in cases in which, as Blakeslee and we have reported elsewhere,[17] a unilateral lesion of the vestibular nuclei still produced unilateral vestibular signs, even though the labyrinth or the eighth nerve had previously been destroyed on both sides.

Cerebellar Dysfunction.—Table 3, as compared with table 2 summarizes the typical findings observed as a result of purely cerebellar lesions. We must recall here that the term "cerebellar" as used in this study applies merely to structures of probably pure cerebellar nature and not to such structures as the juxtarestiform system or the roof

16. Rademaker, G. S. J.: Reactions labyrinthiques et équilibre, Paris, Masson & Cie, 1935.

17. Ferraro, A.; Barrera, S. E., and Blakeslee, G. A.: Vestibular Phenomena of Central Origin, Brain **59**:466, 1936.

nuclei, which are apparently involved in mediation of impulses of vestibular and cerebellar origin. When we limited ourselves to the symptoms seen in monkeys with lesions of such cerebellar structures, including the lateral lobe, the dentate nucleus, the inferior cerebellar peduncle and, as a rule, the superior cerebellar peduncle, we found symptoms which could easily be distinguished from those seen in animals with vestibular lesions. In such cases we did not find postural asymmetries in the sense of torsion of the head or relative flexion or extension of the limbs of the two sides. As a rule, animals with cerebellar lesions showed no asymmetries in posture, if we may discount the pseudopostural deficiency in the limbs, which may have been due to differences in tonus or inability to control properly the limbs in movement. As a rule, animals with cerebellar lesions, in the sense in which we have used the term, showed a normal, symmetrical posture of the head.

In contrast to the asymmetries in movement of the body as a whole around a chosen axis, which were the rule in the animals with vestibular lesions, animals with cerebellar lesions presented no such abnormalities. The "cerebellar" animal, when allowed to fall, usually actively attempted to regain its balance, and did so relatively effectively. Likewise, such an animal climbed symmetrically, and in jumping did not show any tendency to spiral or rotate about a particular axis.

In addition, the "cerebellar" animal was capable of swimming under water in a symmetrical fashion, with no danger of drowning. Even completely decerebellated monkeys were capable of relatively normal swimming under water.

Abnormalities in movements of the eyes were not usual in animals with cerebellar lesions. We did not find true spontaneous nystagmus in the resting position in any animal with a pure cerebellar lesion. To be sure, in animals with complete removal, and in some with wide destruction, of the cerebellum, a certain amount of nystagmus in any direction of gaze may be observed. However, this is not true spontaneous nystagmus in the resting position, which is found as a rule in association with lesions of the vestibular system. Likewise, we did not see incoordination of ocular movements, or abnormalities in induced nystagmus, in the sense of asymmetrical responses, in animals with pure cerebellar lesions. The only finding in animals with cerebellar lesions which might be called an abnormality in induced nystagmus was a tendency toward prolonged response after rotation or caloric stimulation. Even this, however, although common, was not necessarily a constant feature. Vertical nystagmus in the resting position was not seen in any animal with a pure cerebellar lesion.

In contrast to the absence of incoordination of movements between different parts of the limbs or of the limbs and the trunk in animals with

vestibular lesions, we found that such abnormalities were the rule in animals with cerebellar lesions, that is, if any effect was manifested. Large lesions of the cerebellum, especially of the lateral lobes, without involvement of the dentate nuclei could be made without any noticeable incoordination of muscular movement. However, when lesions extended deep enough to involve the dentate nuclei, the phenomenon which one may classify as ataxia, dysmetria or asynergia usually developed. As compared with animals with vestibular lesions, in which apparent dysmetria could be eliminated by immobilizing the rest of the body, the disability persisted in animals with cerebellar lesions. In the latter, for example, the dysmetria might be manifested in reaching movements of the right foreleg. The disability persisted even if the trunk and head were held immobile in the symmetrical position. This seems to indicate that the effect of cerebellar lesions, if manifested at all, is due to a localized process involving apparently the activity relationships of muscle groups rather than the activity of the body as a whole with reference to any axis in space.

Changes in muscular tonus and tendon reflexes in the "cerebellar" animals were as a rule difficult to delimit accurately, but in general some degree of ipsilateral hypotonia or hyporeflexia occurred in association with a unilateral lesion. However, the hypotonia did not occur in cases in which the cerebellum was completely removed or in which the destruction was extensive and involved both sides.

Vestibular and Cerebellar Dysfunctions.—In a consideration of the general symptoms referable to lesions of structures of the third type, namely, those embodying vestibular and cerebellar relationships, attention is first focused on the periventricular structures, particularly the roof nuclei and the juxtarestiform fibers. As we reported elsewhere,[18] in cases of lesions of these structures, for example, the juxtarestiform fibers, the predominant elements in the symptoms appeared to be "vestibular." The symptoms may best be classed as "vestibular" because they resembled in type those observed in cases of known vestibular lesions. In such cases, postural defects, spontaneous nystagmus and asymmetry of motion of the body as a whole occurred. As already reported, the direction of these symptoms was the reverse of that in cases of lesions of the primary vestibular nuclei, vestibular nerve or labyrinth. The magnitude was markedly less. If the lesion was confined strictly to either the roof nuclei or the juxtarestiform fibers, there was not definite ataxia or dysmetria, which were cardinal features of pure cerebellar lesions. If the lesion of the roof nuclei, for example,

18. Ferraro, A., and Barrera, S. E.: The Effects of Lesions of the Juxtarestiform Fibers (I. A. K.) in Macacus rhesus, Arch. Neurol. & Psychiat. **35**:13 (Jan.) 1936.

extended dorsally so as to catch some terminal fibers of the spinocerebellar tracts, an additional cerebellar element was introduced, manifested possibly by ataxia. This also occurred if the lesion of the juxtarestiform fibers extended laterally so as to involve the fibers as they emerged from the dentate nucleus to form the superior cerebellar peduncle. Recent findings of Keller and his co-workers [19] have tended to confirm the observation that the symptoms associated with lesions of the vermis tend to be more prominent than those associated with lesions of any purely lateral cerebellar structures. Dow [20] also reported a "vestibular" group of phenomena associated with lesions of the uvula and nodules. In our cases, lesions of the purely cortical portions of the vermis, including the uvula and nodules, and of the cortical portions of the central or anterior portions of the vermis were not associated with symptoms which we could class as "vestibular." On the other hand, they were associated with marked instability of the trunk, which we prefer to consider as evidence of truncal incoordination or asynergia. However, if the lesions were large and deep, involving the roof nuclei, the disability was much more severe and might involve other elements which can be considered as "vestibular," including transient vertical nystagmus and a tendency to *Stutz* tonus, with falling backward on climbing and jumping forward and upward. Lesions of the vermis, therefore, demonstrate combined effects of vestibular and cerebellar lesions.

COMMENT

In light of the brief summary presented, it seems that there are, or should be, definite points of differentiation between pure cerebellar and pure vestibular lesions. This would probably be true if lesions, as usually encountered experimentally or clinically, were limited to either purely vestibular or purely cerebellar structures. Such, however, is not the case. In the average clinical case, in which, for example, there is a destructive lesion or a neoplasm in the posterior fossa, it is usual to observe that the pathologic process has involved elements of both cerebellar and vestibular type, either directly or by pressure, thus introducing complicating features into the case. The same is true of the majority of experimental investigations. Much of the experimental work on the cerebellum has been done either by hemidecerebellation or complete decerebellation. Aside from the possibility that in such operations the primary vestibular centers may be directly involved by the

19. Keller, A. D.: Personal communication to the authors and demonstration at the meeting of the American Physiological Society, Memphis, Tenn., April 21-24, 1937.

20. Dow, R. S.: The Effects of Removal of Vestibular Parts of the Cerebellum in Primates, Am. J. Physiol. **119**:42, 1937.

lesion, there is always the certainty that structures such as the juxtarestiform system will be involved in addition to definitely cerebellar structures, thus introducing combined vestibulocerebellar effects. This is not true of large experimental lesions alone. In many cases of supposedly isolated lesions of the cerebellar peduncles, such as those reported by Ferrier and Turner and others,[21] symptoms were reported which we observed [22] only if the lesion of the restiform body extended beyond this structure in such a way as to involve the vestibular nuclei. It is possible now to disentangle such complicated symptom complexes and to delimit to a certain extent the elements, such as rolling or marked postural differences, which are vestibular and those, such as ataxia or dysmetria, which appear to be of cerebellar origin.

Indeed, it is not always possible to deduce symptoms which one might expect as the result of a combined lesion of two systems merely from a sum of the symptoms associated with a lesion of each of the two systems. For instance, resting, shaking tremor does not occur in monkeys with section of the restiform body alone. It likewise does not occur in animals with puncture lesions of the descending vestibular root. However, in cases in which the lesion is produced in such a manner as to involve both these regions to some extent, the tremor as a rule develops. In addition, the rolling movements, so commonly reported for unilateral lesions of the inferior cerebellar peduncle by earlier experimenters, are not found if the restiform body alone is sectioned in the monkey. In addition, they do not occur as a rule with vestibular lesions alone unless the lesion is large and involves a considerable portion of the primary vestibular nuclei, especially the descending group or Deiters' nucleus. However, if a combined lesion involves the restiform body and a relatively small portion of the primary vestibular nuclei, a violent rolling movement occurs as a rule. In addition, in such cases there is nystagmus, which does not appear after simple, uncomplicated lesions of the restiform body. Likewise, the postural asymmetries do not appear unless the lesion is complicated in the sense of involving both the systems to some extent.

In order to investigate the effects of addition of vestibular and cerebellar components even within the gross mass of the cerebellum, attempts were made with a few animals to remove or section all the purely cerebellar structures, including the dentate nuclei, the middle and inferior

21. Ferrier, D., and Turner, W. A.: A Record of Experiments Illustrative of the Symptomatology and Degenerations Following Lesions of the Cerebellum and Its Peduncles and Related Structures in Monkeys, Phil. Tr. Roy. Soc., London, s.B **185**:719, 1895.

22. Ferraro, A., and Barrera, S. E.: The Effects of Lesions of the Dorsal Spino-Cerebellar Tract and Corpus Restiforme in the Macacus Rhesus Monkey, Brain **58**:174, 1935.

cerebellar peduncles and the complete cortex, with preservation, however, of the roof nuclei and the juxtarestiform system. Although at this time we are not prepared to state exactly the histologic status in these cases, we can say that the clinical symptoms were far from being as intense, or even of the same type, as those in animals with complete removal of the cerebellum. Whereas our monkeys with complete removal of the cerebellum did not in some cases walk for a long time after removal of the cerebellum, the animals with the lesions just mentioned were able to walk soon after the operation. In addition, they did not manifest the severe shaking, forced movements usually seen in an animal with complete removal of the cerebellum. They showed a considerable degree of ataxia or dysmetria, but this was not as severe as that in animals with complete removal of the cerebellum. In addition, the rapid exhaustibility, so characteristic of completely decerebellate animals, was not as marked in our monkeys, in which the periventricular juxtarestiform-roof nuclear system was preserved. We are forced to conclude as a result of these experiments that the additional features due to section of the juxtarestiform system in cases of complete decerebellation are responsible for certain new elements and the intensification of others in the symptom complex associated with complete removal of pure cerebellar structures.

Considerable light on the relative independence of the cerebellar and the vestibular system has been afforded by the careful experimental work and clinical observations of Magnus [15a] and of Rademaker [16] and his co-workers. Magnus and his group showed that the various postural reflexes usually ascribed to vestibular function are relatively independent of the cerebellum. Rademaker and his co-workers studied intensively the application of certain tests to patients and animals with various known vestibular and cerebellar lesions. In general, they found that the tests devised to study the various vestibular postural reflexes gave normal results in cases of supposedly pure cerebellar lesions—in fact, even in cases of wide destructive lesions of the cerebellum—whereas definite abnormal results could be obtained in cases of various types of lesions of the vestibular system, such as a dead labyrinth or vestibular nerve. It is common knowledge that in many cases in which a pathologic lesion is associated with definite clinical symptoms referable to the cerebellum, central structures, such as the vermis, are involved. In these cases, of course, direct involvement of cerebellar and vestibular elements is present. It is also known that in many cases of a pathologic lesion in the lateral lobe relatively little may be shown. Many investigators of the cerebellum have reported definite findings which we believe are suggestive of vestibular involvement, such as postural asymmetries of the head and nystagmus, but in general little adequate anatomic control has

been presented in these cases. When a neoplasm is involved there is always a possibility of the effect of transmitted pressure on the vestibular nuclei.

Our controlled experiments to date have convinced us that a certain set of symptoms and findings are associated with lesions of pure cerebellar type. In addition, another group of findings exists in cases of lesions of pure vestibular structures. In the monkey it is possible for us, if either of these groups of findings occurs, to diagnose a lesion of a pure cerebellar or of a pure vestibular structure. The more common condition in the monkey involves, however, some combination of vestibular and cerebellar elements, owing usually to inclusion of both these systems in a complicated lesion. In such cases it appears necessary to hypothecate a cerebellovestibular or a vestibulocerebellar syndrome, analysis of which becomes of interest and importance if one is to speak of the function of any part, such as the gross cerebellum.

SUMMARY

1. A study has been made of the clinical symptoms associated with lesions of various portions of the structures in the posterior fossa in over 300 Macacus rhesus monkeys. An attempt was made to ascertain the symptoms referable to vestibular, to cerebellar and to combined vestibulocerebellar lesions.

2. The lesions, all anatomically controlled by serial sections, involved three types of structures: those known to be vestibular, those known to be purely cerebellar and those known to be connected anatomically with both the cerebellar and the vestibular system. Structures in the first group of lesions included the labyrinth, the eighth nerve, the primary vestibular nuclei and the posterior longitudinal bundle. Those in the second group included the various portions of the cerebellar cortex, the lateral lobe, the dentate nucleus and the inferior, middle and superior peduncles. Those in the combined group included the juxtarestiform fibers, the roof nuclei and all lesions involving these structures, including hemidecerebellation, complete decerebellation and removal of large portions of the vermis.

3. Lesions of purely cerebellar structures were associated with symptoms which appeared to be related mainly to muscular incoordination of a particular portion of the body, depending on the part of the cerebellum involved. Ataxia and dysmetria with inconstant and variable hyporeflexia and hypotonia were the rule with small, unilateral lesions. With large, bilateral lesions the hypotonia did not occur.

4. Lesions of purely vestibular structures were associated clinically with a group of symptoms which seemed to be characteristic and served to differentiate animals with a lesion of this type from those with purely

cerebellar lesions. The syndrome included: postural asymmetries; asymmetries in movement of the body as a whole, especially in homogeneous mediums such as air and water; spontaneous nystagmus; abnormalities in induced nystagmus; abnormalities in position and labyrinthine reflexes, and inconstant, variable changes in muscular tone and tendon reflexes. Ataxia was not present.

5. Lesions of the roof nuclei and juxtarestiform system were associated with predominantly vestibular features. Lesions of combined known vestibular and cerebellar structures were associated clinically with symptoms referable to both these systems, including all the symptoms seen in animals with vestibular lesions and, in addition, some ataxia or dysmetria. In addition, there were other features, such as tremors, which were not present with simple lesions. It seemed that the two combined lesions were often associated with symptoms not found as a rule with lesions of either of the two systems alone.

6. As a result of the experiments, it was possible, in monkeys at least, to differentiate clinically animals with cerebellar and those with vestibular lesions, thus simplifying the symptom elements associated with lesions of the gross cerebellum.

SENSORY DISCRIMINATION IN MONKEY, CHIMPANZEE AND MAN AFTER LESIONS OF THE PARIETAL LOBE

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The problem of localization of function in the parietal lobe remains essentially as it was two or three decades ago.[1] The results of the many clinical studies and the few animal experiments, excellently executed and employing a variety of ingenious methods, disagree with respect to many features of the localization of somatic sensory function. The extent of the cortex involved in somatic sensation and the extent of the role played by the thalamus at various phylogenetic levels are still uncertain, as is the question of bilateral representation. It is not known whether different modalities of somatic sensation are separately localized over the face of the cortex or whether, as is a priori more likely, levels of sensory response are separately represented. It is perhaps significant that in recent years no diagram maker has had the temerity—and diagram makers do not usually lack that quality—to offer a functional map of the sensory cortex.

There are many reasons that knowledge of somatic sensory localization has been gained slowly. One is the difficulty of studying somatic sensory disturbances, which is magnified by the number of sense modalities, each having several levels of sensation, that must be taken into account. Another is that the parietal lobe has not shared the advances made possible in other cortical spheres by extensive and circumscribed lobectomy.

The observations to be discussed are the first results of an attempt to study, objectively and quantitatively, the cortical mechanism underlying cutaneous and muscle sensibility in the chimpanzee and in man. Ulti-

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1. Head, H.: Sensation and the Cerebral Cortex, Brain **41**:57-253, 1918.

mately it should be possible to trace the phylogenetic changes in "corticalization" and in the concentration of representation within the cortex through monkey and chimpanzee to man. The study of the parietal lobe from a phylogenetic point of view is of particular interest because in man somatic sensation appears to be less corticalized and less focally represented than are the teleoceptive functions, e. g., vision. The experimental studies of animals, particularly of the higher primates, must therefore influence considerably one's view on function of the parietal lobe until a sufficient series of extensive and restricted surgical excisions of known extent and position have been studied quantitatively.

REVIEW OF LITERATURE

Anatomic and physiologic evidence both indicate that a relatively large area of the primate cortex is concerned with somatosensory function. According to Poliak [2] the "minimal somatic sensory region" of the macaque's cortex extends over almost the whole of the motor and premotor cortex (areas 4 and 6) and of the parietal lobe (areas 3, 1, 2, 5 and a considerable portion of 7); the projection is more dense in the depths of the central fissure and thins out progressively toward the anterior and posterior boundaries. Walker [3] has resolved this area into three subareas, each with a different type of sensory projection. That to the precentral region is derived from a thalamic nucleus which receives fibers from the superior cerebellar peduncle. The postcentral gyrus is in direct receipt of fibers from the nuclei in which the great ascending sensory systems terminate. The thalamic nuclei which project to the posterior parietal lobule are secondary nuclei; i. e., they receive no direct fibers from the ascending sensory tracts but are connected with other thalamic nuclei. Thus the postcentral gyrus is most directly connected with the sense organs, a fact in keeping with the known topographic representation in this gyrus. The more anterior and posterior cortical regions presumably receive impulses that have already undergone some degree of correlation.

The well known strychnine experiments of Dusser de Barenne [4] likewise suggested an extensive somatosensory area. Stimulation of the cerebral cortex by strychnine anywhere between the arcuate fissure and the parietal fissure induces positive sensory symptoms—paresthesia, hyperalgesia and hyperesthesia. For cutaneous sensation, but not for deep sensibility, this overresponse is manifested bilaterally from stimulation of one hemisphere. The careful observations of Minkowski [5] on the monkey implicated an equally extensive area. He found areas 4 and 6 as well as the whole of the parietal lobe to be concerned with deep sensibility. Complete bilateral parietal lobectomy and lesions of component areas failed

2. Poliak, S.: The Main Afferent Fiber Systems of the Cerebral Cortex in Primates, Berkeley, University of California Press, 1932.

3. Walker, A. E.: The Thalamus in Relation to the Cerebral Cortex, J. Nerv. & Ment. Dis. **85**:249-261, 1937.

4. Dusser de Barenne, J. G.: Experimental Researches on Localization in the Cerebral Cortex on the Monkey (Macacus), Proc. Roy. Soc., London, s.B **96**:272-291, 1924.

5. Minkowski, M.: Étude sur les connexions anatomiques des circonvolutions rolandiques, pariétales et frontales, Schweiz. Arch. f. Neurol. u. Psychiat. **1**:389-459, 1917; **12**:227-268, 1923; **14**:255-278, 1924; **15**:97-132, 1924.

to produce anesthesia of any sense modality, although certain higher levels of sensation (localization) were completely abolished. The study of hopping and placing reactions by Woolsey and Bard [6] indicated a somewhat restricted localization of these functions. Contact "placing" is permanently lost after parietal lobectomy, while the hopping reaction, though initially severely affected, eventually returns to normal. Since this reaction is dependent on the motor cortex, it was reasonably inferred that the motor cortex also serves the sensory aspect of the reaction. A fuller review of the experimental literature on the cortical localization of somatic sensory function will be found in the paper by Ruch and Fulton.[7] The clinical literature was discussed from a physiologic point of view by Pieron;[8] no recent comprehensive review has appeared.

METHODS OF STUDY

An obvious difficulty in investigating the cortical localization of sensory processes in animals is in knowing what sensations an animal experiences. We have sought to meet this difficulty by employing one of the training technics of the comparative psychologist—the discrimination method of Yerkes and Watson. It has proved possible to train monkeys and chimpanzees to discriminate between weights of different magnitude, between patches of emery paper of different roughness and between various geometric solids. In this case it is necessary to know nothing of what the animal experiences but only that stimuli differing by certain amounts are or are not distinguished.

Discrimination of Weight.—At each trial the animal is confronted with two cylinders of unequal weight. The chimpanzee is taught that if the lighter weight is withdrawn and placed in the weight-receiving chamber a bit of food is forthcoming; selection of the heavier weight is unrewarded. The cylinders and the contained weights are shifted independently from side to side in a random order to prevent successful discrimination on the basis of visual or position cues. Typically, the weights are "hefted" alternately ("sampling") several times before one is selected; as many as forty "lifts" in one trial have been recorded.

Discrimination of Roughness.—For tactual discrimination the animal rotates drums covered with two grades of emery paper. Complete rotation of the drum bearing the smoother emery paper electrically releases food to the animal. This test is performed in darkness to avoid visual discrimination, and the drums are interchanged in a chance order.

Discrimination of Shape.—The pair of geometric solids to be discriminated are placed in a deep canvas bag from which the animal must select the correct form by palpation in order to receive food.

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6. Woolsey, C. N., and Bard, P.: Cortical Control of Placing and Hopping Reactions in Macaca Mulatta, Am. J. Physiol. **116**:165, 1936.

7. Ruch, T. C., and Fulton, J. F.: Cortical Localization of Somatic Sensibility: The Effect of Precentral, Postcentral and Posterior Parietal Lesions upon the Performance of Monkeys Trained to Discriminate Weights, A. Research Nerv. & Ment. Dis., Proc. **15**: 289-330, 1935.

8. Pieron, H.: Thought and the Brain, New York, Harcourt, Brace and Company, Inc., 1927.

Clinical Cases.—Four patients with lesions in the parietal region were studied by methods essentially similar to those employed with animals. Quantitative results were obtained on the discrimination of weight with the hand supported (pressure) and unsupported (muscle and tactual senses) and on the discrimination of grades of emery paper (roughness). Semiquantitative observations were made on topognosis, sense of position, two point discrimination, stereognosis, figure writing, etc.

CASE 1.—J. P., a white youth aged 18, was admitted to the hospital on Sept. 2, 1935, ten months after a spontaneous subarachnoid hemorrhage. During this interval there had been visual hallucinations of white and colored lights referred to the right eye, headaches, blurring of vision and stiffness of the neck. Neurologic examination revealed bilateral papilledema, rigidity of the neck and a cautious gait. The sensory examination and the visual fields were normal. Right occipital craniotomy disclosed an aneurysm of the posterior cerebral artery, with a hemorrhagic cyst in the anterior portion of the occipital lobe. The posterior portion of the right cerebral hemisphere was resected in a curvilinear line which crossed the calcarine fissure 4 cm. anterior to the occipital pole, extending anteriorly and laterally to a point in the midparietal region 8 cm. anterior to the occipital pole and thence slightly posteriorly, beneath the temporo-occipital region to the median sulcus. The excised portion contained 3.5 cm. of the lateral ventricle.

CASE 2.—L. S., a white man aged 57, was admitted to the hospital on Jan. 13, 1936, with a history of peripheral vascular disturbance for four years. For three weeks preceding admission there had been left frontoparietal headaches, numbness and awkwardness of the right hand and constriction of the visual field of the right eye. Neurologic examination revealed bilateral papilledema, moderate aphasia, defective appreciation of all forms of sensation in the right hand and concentric constriction of the right visual field. At operation a thrombotic infarct, 2 cm. in diameter, was identified in the left superior parietal region, extending into the postcentral gyrus in the region of the hand area. The localization was confirmed by electrical stimulation of the motor and sensory cortex.

CASE 3.—G. D., a white youth aged 18, was admitted to the hospital on June 5, 1931, one week after a mild head trauma. The symptoms were headache, drowsiness, convulsions and weakness on the left side. The significant signs were left hemiplegia and hemianesthesia, hyperactive reflexes and a positive Babinski reaction on the left. A subcortical hematoma was evacuated through an incision 3 cm. in length through the right precentral gyrus, at the level of the second and third frontal convolutions. Convulsions necessitated a second operation on Aug. 2, 1933. A cortical scar, 5 cm. in diameter, was excised from the precentral and postcentral gyri, extending down to the wall of the lateral ventricle.

CASE 4.—A. M., a white man aged 29, was admitted to the hospital on Feb. 2, 1937, nine years after a severe cranial trauma. For the past four and one-half years there had been convulsions. Neurologic examination revealed a sensory defect in the left hand, minimal atrophy of the left hand and forearm, left homonymous hemianopia and nystagmus. Encephalography demonstrated a porencephalic cyst replacing the right occipital lobes and extending anteriorly to a point 4.5 cm. behind the coronal suture.

EXPERIMENTAL RESULTS

Monkeys.—Discrimination of lifted weights was tested in a series of monkeys subjected to three types of cortical lesion: unilateral lesion (incomplete) of the precentral gyrus; bilateral lesion of the posterior

parietal lobe, and bilateral extirpation of the postcentral gyrus.[7] In each case the performance several weeks [9] after operation duplicated the preoperative level. After postcentral operation some impairment was noticed in the first days of retesting, but even this transitory defect was slight. From these experiments it was concluded that the discrimination of weight is not focally represented in the cerebral cortex and that it is subserved either by a wide extent of precentral and postcentral cortex or by the thalamus. Attempts to combine lesions of the parietal and frontal lobes resulted in all animals in a degree of paralysis and ataxia which left the animal unable to carry out the requisite manipulations of the weights. In one animal, however, destruction of the anterior wall of the central sulcus added to an earlier ablation of the postcentral gyrus was not productive of disturbance of weight discrimination. On the other hand, a lesion which included the posterior parietal lobule as well as the postcentral gyrus induced marked and permanent ataxia and severe initial disturbance of weight-discriminatory ability, which lessened but persisted despite extensive training. The effect of unilateral parietal lobectomy on the discrimination of grades of emery paper was rather similar. Finer differences were not discriminated with the accuracy exhibited in preoperative tests. However, the discrimination of larger differences was unaffected.

Chimpanzees.—The parietal lobe of the chimpanzee represents a considerable advance over that of the monkey with respect to area and complexity of the fissural pattern. This is manifested in the greater development of the superior postcentral fissure, the fragmentation and horizontal course of the intraparietal fissure and the expansion of the region of the angular and supramarginal gyri. These gyri, however, are markedly less developed than those of the human cortex. With this morphologic development is to be expected an increase in the importance of the parietal lobe to somatic sensory function. This expectation is to some degree realized in the following experiments on the localization of function in the chimpanzee cortex.

Discrimination of Roughness.—In figures 1 and 2 is shown the ability of the chimpanzee to discriminate between grades of emery paper before and after various lesions of the parietal lobe. The graphs show the percentage of trials (ordinates) in which successively smaller differences in roughness (abscissas) were successfully discriminated. Triple 0 emery paper was the "standard" and the "positive" stimulus in all experiments. On the extreme left is given the performance in discriminating between the "standard" and a fine nutmeg grater. It should be kept in mind that the trials which were 50 per cent correct

9. Paralysis and ataxia forbid early postoperative testing of the animals. In any case early testing was avoided on principle.

represent complete failure to discriminate, because that is the performance to be expected in a purely chance selection.

The striking result of these experiments (fig. 1 *A* and *B*) is that neither lesions of the postcentral gyrus nor those of the posterior parietal

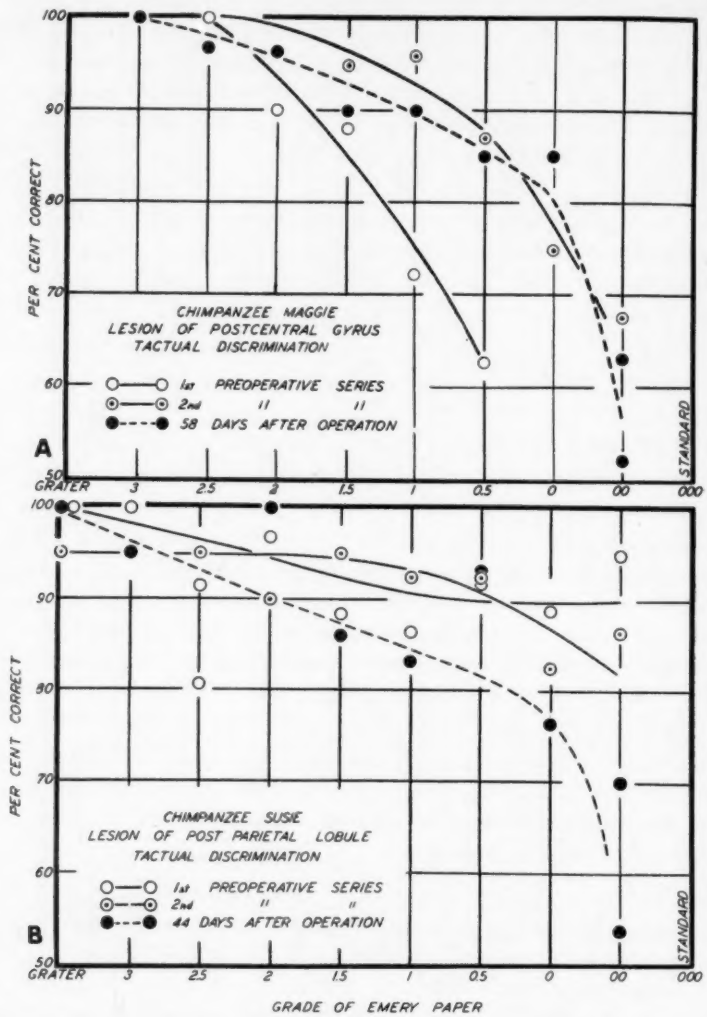

Fig. 1.—*A*, training record showing the percentage of trials (ordinates) in which successively smaller grades of emery paper were successfully discriminated from triple O grade by chimpanzee Maggie after a lesion of the postcentral gyrus (complete except for 3 mm. of the anterior wall of the inferior postcentral sulcus) contralateral to the hand tested. *B*, discrimination of emery paper with the hand contralateral to a lesion of the posterior parietal lobule, secondary to ipsilateral complete parietal lobectomy. There is a suggestion of postoperative deficit in the discrimination of OO and OOO emery paper.

lobule produced any significant, permanent lessening of discriminatory ability. In the case of the chimpanzee Susie, in which the posterior parietal lobule contralateral to the arm tested was extirpated after a complete parietal lobectomy on the opposite side, there was a suggestion of decreased ability to discriminate the smaller differences in grade of emery paper. Other experiments made certain that any existing difference would disappear with further training. Lesion of the postcentral gyrus in chimpanzee Maggie (fig. 1 *A*) was totally without effect; in chimpanzee Tommie (fig. 2 *A*) it produced a striking disturbance in the first preoperative series, but with continuation of training the preoperative level of ability was regained.[10] It is clear from these three experiments that the discrimination of roughness is not focally represented in either the anterior or the posterior division of the parietal lobe.

Figure 2 *A* shows the effect of removal of the posterior parietal lobe consecutive to ablation of the postcentral gyrus. This resulted in "renewal of symptoms," but with extensive retraining the preoperative level of performance was virtually recaptured. Figure 2 *B* shows the effect of a complete parietal lobectomy in one stage in the chimpanzee Susie. Here the initial disturbance was greater and the degree of recovery was considerably less. The difference between figure 2 *A* and figure 2 *B* is in the degree of recovery; in neither case is the discrimination abolished. There still remains a discrepancy which only further lobectomy experiments can clear up;[11] yet the two experiments taken together indicate clearly that the neural mechanism underlying this type of discrimination is not confined to the parietal lobe of the cerebral cortex contralateral to the hand tested.

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10. Analysis of the daily score for Maggie indicates that recovery with retraining occurred within the threshold series and kept pace with the increasing difficulty of the problem. The discrepancy between the two animals is in the rate of recovery, not in residual ability. This, it is believed, is accounted for by the extent of the lesions. In Maggie, preliminary histologic examination has shown that the lesion, though accurately splitting the floor of the central fissure, spared from 3 to 4 mm. of depth of the anterior wall of the postcentral fissure. Moreover, histologic and neurologic examination suggested that Tommie suffered greater accidental damage of area 4. Whether this is significant because of the further reduction of thalamocortical projection or because of the increased ataxia and motor weakness is still undecided.

11. It is certain that the results obtained on Susie overestimate the role of the parietal lobe in this function. The degree of paralysis and rigidity in the fingers and the ataxia of the movements of the arm exhibited by this animal as an enduring symptom must certainly limit the performance in any problem requiring accurate manipulation without visual guidance. The extent of the damage to the arm area of the motor cortex in Tommie, together with the fact that motor disturbances were far greater in Susie, suggests that autopsy will prove the lesion in the latter animal to be a complete parietal lobectomy and nearly complete destruction of the arm region of area 4.

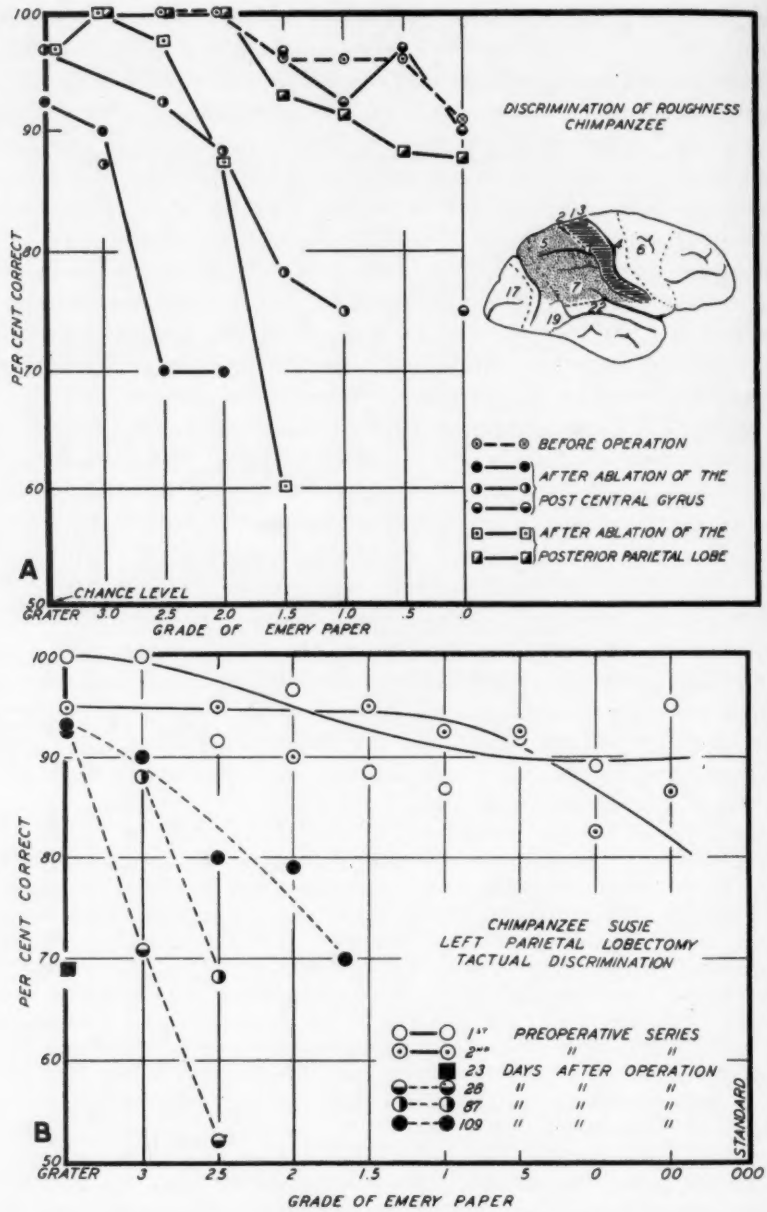

Fig. 2.—*A*, discrimination of emery paper after ablation of the postcentral gyrus of chimpanzee Tommie and after subsequent extirpation of the posterior parietal lobe. Note recovery after the first lesion, renewal of symptoms after the second and subsequent return to the preoperative level. *B*, discrimination of emery paper with the right hand after ablation of the left parietal lobe (with probable damage to the arm region of the motor area).

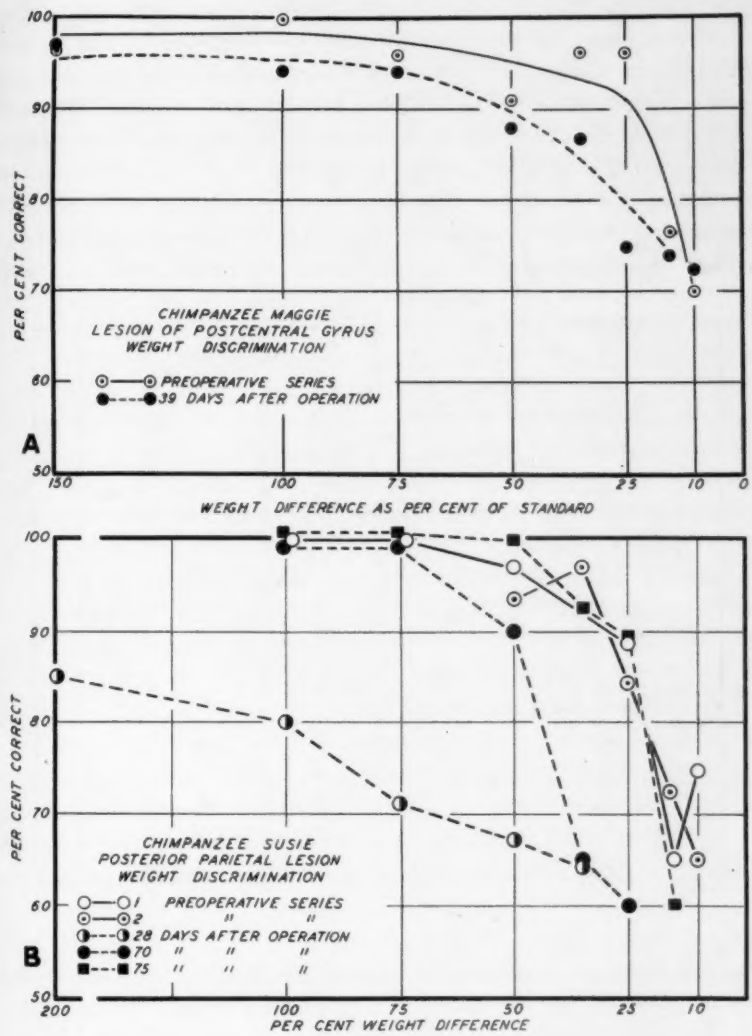

Fig. 3.—*A*, discrimination of lifted weights after lesion of the postcentral gyrus. The points on the postoperative curve for 10 and 15 per cent are based on a large number of trials and establish the absence of any significant reduction in postoperative ability. *B*, discrimination of lifted weights after ablation of the posterior parietal lobule contralateral to the arm tested, secondary to ipsilateral parietal lobectomy. Note the decreased ability shown in the first postoperative series; the flatness of this curve is probably due to "recovery and relearning" within a series (see text). The improvement between the second and the third postoperative curve (filled circles and squares) is due to retraining, the lapse of time being insignificant.

Weight Discrimination.—A study of the weight-discriminatory ability after parietal lesions yielded broadly similar results to those already described for the discrimination of roughness. This is illustrated in graphs similar to those previously shown except that they indicate the percentages of successful discriminations at successively smaller weight differences. The weight differences are expressed as percentages of the standard weight of 100 Gm. (Weber's fraction). It is apparent from figure 3*A* (Maggie) that an extensive lesion of the postcentral gyrus has relatively little effect on weight-discriminatory ability, as was the case for discrimination of roughness. Ablation of the posterior

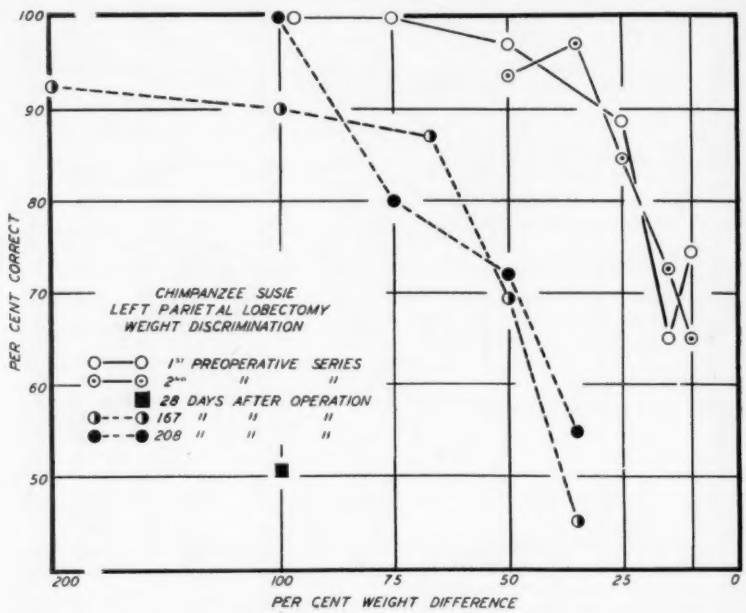

Fig. 4.—Discrimination of lifted weights after parietal lobectomy. Discriminatory ability was tested later after operation (except for retention test, filled square) than in other experiments, owing to motor disturbances.

parietal lobule (Susie, fig. 3*B*) induced a severe initial deficit, but with lapse of time and further training the preoperative level was virtually attained. These two experiments taken together perhaps suggest that the posterior region is more concerned with weight discrimination than is the postcentral gyrus. The effect of parietal lobectomy (Susie, fig. 4) was both more profound initially and more permanent. Twenty-eight days after operation the animal failed completely (solid square) on a large weight difference. The curves for the two postoperative threshold series approach the chance level at weight differences which were nearly

perfectly discriminated before operation.[12] It is significant that this is the only instance in which repetition of a threshold series (retraining) failed to produce a significant improvement.

The three experiments together suggest that weight discrimination is not subserved by any restricted region of the parietal lobe and that this lobe is not the sole region of the brain capable of carrying out such discriminations. It does, however, play an important part in these discriminations.

Discrimination of Three Dimensional Forms.—This type of test was carried out in only one animal. Before operation chimpanzee Susie was taught to discriminate [13] by palpation between a pyramid and a cone and between a pyramid and a wedge. A priori, the discrimination of a pyramid and a wedge would seem the more difficult of the two problems; it proved much the more difficult habit to establish. Working with the hand contralateral to the posterior parietal lesion, Susie was unable to discriminate between the pyramid and the cone in the first postoperative trials. Visual discrimination of the two objects was perfectly retained. With retraining the ability to discriminate was recaptured, and in the end twenty consecutive trials without error were accomplished. However, after extensive retraining in the discrimination of pyramid and wedge, no significant improvement over a chance level of performance has been manifested. It would seem, then, that the lesion induced only partial inability to discriminate geometric solids, but since the disturbance was not dissipated by retraining, the experiment definitely implicates the posterior region of the chimpanzee cortex in what is presumably a higher level of response than the other discriminations studied. It has not been possible to test in this animal the hand opposite the side of parietal lobectomy because the paralysis left the animal unable to carry out the requisite manipulations without the aid of vision.

CLINICAL CASES

In tracing the phylogenetic history of somatic sensory localization from monkey to men the clinical literature has proved of little service. It is quite impossible to translate the subjective verbal evaluations found in case histories into percentages of successful discriminations of a given difference in weight. We have been unable to find in the literature a

12. The ataxia and paralyses exhibited by this animal probably disturbed the weight tests less than the roughness tests because the former are conducted in light and hence allow visual control of movement.

13. "Discrimination of form or shape" is preferred to the expression "stereognosis." That an animal *discriminates* is data; that it has any conceptual knowledge of form is inferred. Human beings with parietal lesions can often discriminate between two forms when neither can be named or described.

single quantitative determination of weight-lifting ability in cases of parietal lesion in man. In an effort to complete the primate series, four cases of damage to the parietal lobe were studied in a manner similar in

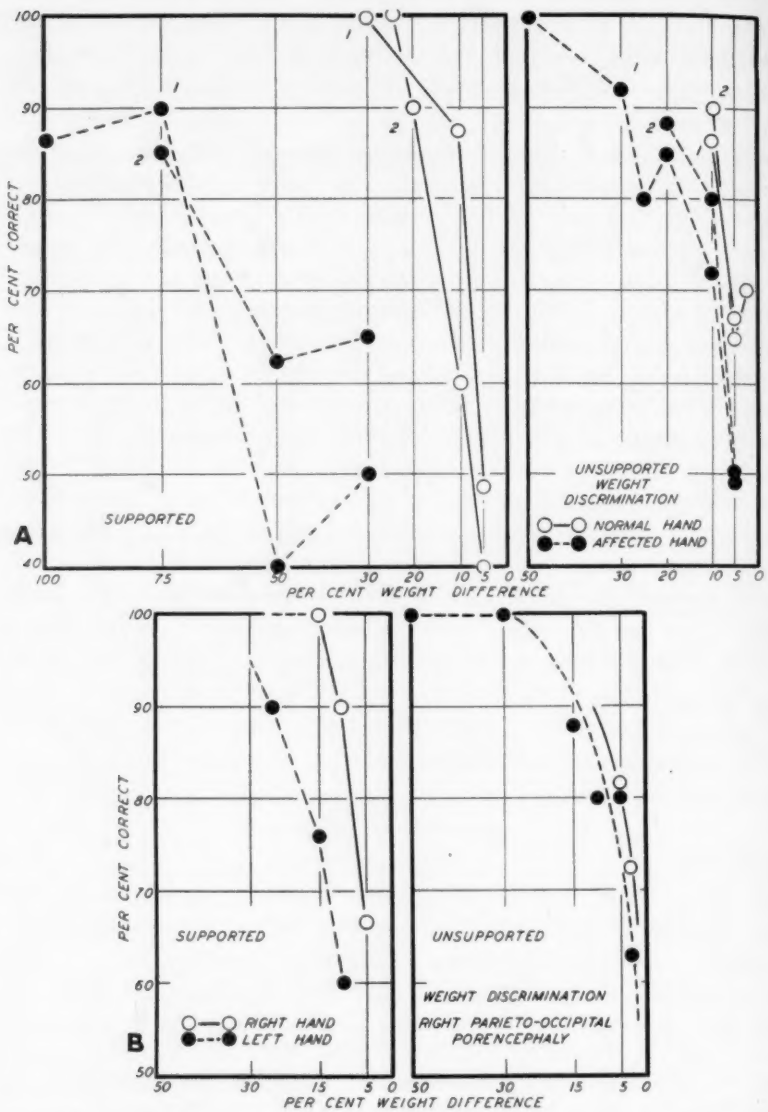

Fig. 5.—Discrimination of supported and unsupported ("free") weight (*A*) in case 1, that of surgical lesion of the posterior parietal lobe in the neighborhood of the intraparietal fissue, and (*B*) in case 4, that of porencephaly involving the occipital and parietal regions, probably congenital in origin. Note the slightness of the reduction of discriminatory ability in the affected hand shown in *B*.

essentials to that in the chimpanzee experiments. Three tests—the discrimination of weights with the hand supported and with the hand unsupported and the discrimination of roughness—were conducted with a sufficient degree of thoroughness to admit of graphic representation.[14]

Discrimination of Weight with the Unsupported Hand.—Figures 5 and 6 show the performance of the normal and the affected hand in discrimination of supported and free weights. For lifted weights there is clear inferiority of the affected hand in three of the four cases. Quantitatively, however, the difference is not great, and considerable discriminatory ability is retained. The weight difference which is discriminated with 70 per cent accuracy by the affected hand is in no case more than twice that for the normal hand. And the difference in the percentage of errors incurred at a given difference in weight is typically less than 25. In none of the cases was the deficit as great as that exhibited by the chimpanzee after complete parietal lobectomy (fig. 4) or in the first threshold series after the more comparable lesion of the posterior parietal lobule (fig. 3*B*). There are, of course, many factors which must be taken into consideration in making such comparisons: the extent of the lesion, the time elapsing after the cortical damage and the amount of retraining. The results suggest that discrimination of lifted weights is more dependent on the cortex, or more focally represented, in man than in the chimpanzee. In the latter, parietal lesions of the parietal lobe at the greatest lead only to disturbances that are eradicated by training and by lapse of time. In man smaller lesions result in more permanent deficits (particularly in case 1). Yet the difference between the two forms would not seem to be great. It is possible that comparable amounts of retraining would further reduce the postoperative incapacity in man. Further, it is significant that relatively large cortical defects in man (cases 3 and 4), particularly when located in the postcentral gyrus, where a topographic representation of the body is known to exist, should show such small deficits.

Discrimination of Supported Weights.—The appreciation of weights placed on the relaxed and supported hand is generally considered to depend on a different set of sense organs than those involved in discrimination of lifted weights. The former depends on pressure receptors, and the latter, on muscle sense and the tactual stimulation by the "drag" of the weights on the skin of the fingers. There is evidence that the tactual

14. These results are published with full knowledge that they fall far short of the accuracy obtained with sophisticated normal subjects by intricate psychophysical methods. Such accuracy need not be the aim of, and in fact may not be possible in, clinical studies. It is hoped, eventually, to adapt psychophysical methods to clinical subjects by some compromise between facility and accuracy, not for routine neurologic examination but for purposes of research.

component does not allow the fine discrimination that is possible with muscle sense. Inspection of the figures suffices to show that in each case discrimination of supported weights is more severely disturbed than

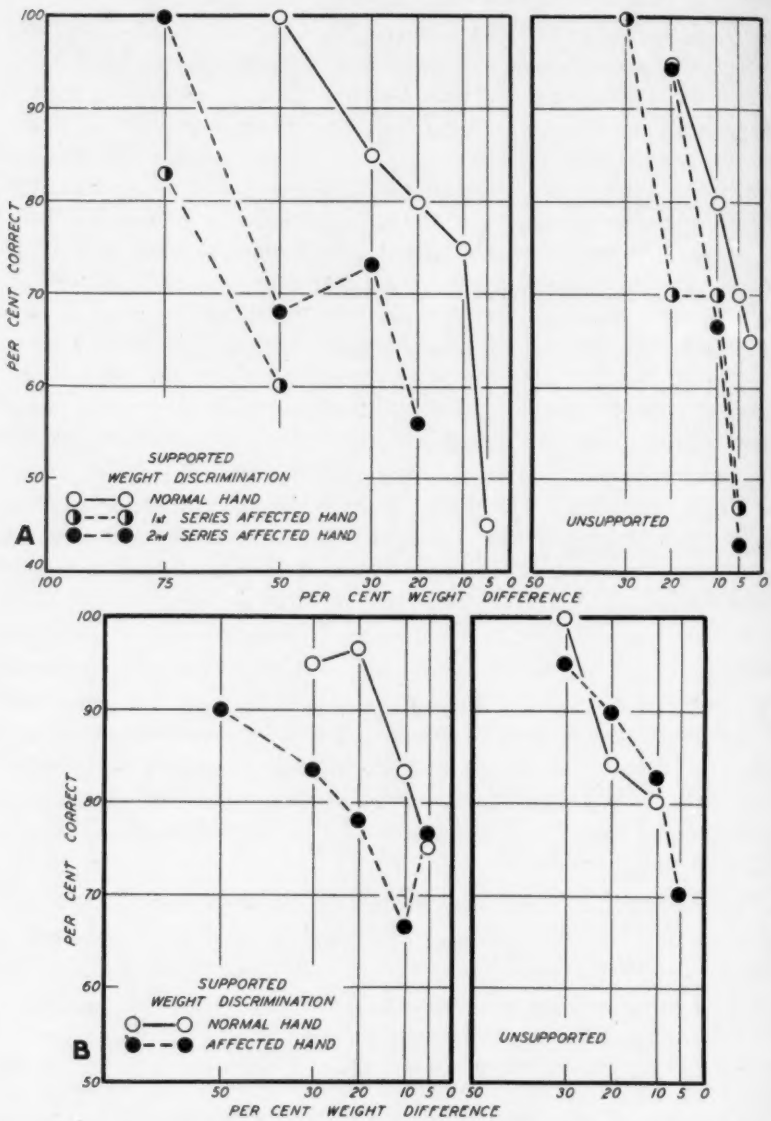

Fig. 6.—*A*, discrimination of weight in case 3, in which the lesion was an excision of a scar in the anterior portion of the parietal lobe. *B*, discrimination of weight, with the hand supported and unsupported, in case 2, in which there was degeneration of the cortex of vascular origin in the posterior parietal lobe, extending into the arm area of the postcentral area.

is that of lifted weights. In making this comparison allowance is made for the fact that the former type of discrimination is less accurate. If the weight difference which is discriminated with 70 per cent accuracy is taken as a comparable point in the two sets of curves, it is seen that the greatest increase in the Weber fraction (weight difference as a percentage of the standard) in the affected hand is in the neighborhood of 100 per cent for the lifted weight; for discrimination of supported weights this is the lowest value, and in other cases the increase is several hundred per cent.[15]

In the two cases in which was exhibited the greatest relative and absolute disturbance in discrimination of supported weights, one lesion was placed posteriorly and the other anteriorly. This suggests that the "dissociation" is probably not based on separate cortical representation of the two sensory processes but that discrimination of supported weights is more dependent on the cerebral cortex. The fact that discrimination of lifted weights has a tactual factor, in addition to the kinesthetic one, may also be responsible in part for its being relatively spared in cases of subtotal lesion of the parietal lobe. The different behavior in the two tests, if confirmed in a more extensive series, would indicate that discrimination of supported weights is a more sensitive test of damage to the parietal lobe. It, of course, has also the great advantage of being applicable to any part of the body and to a paralyzed or an incoordinated arm.

COMMENT

Extent of the Somatic Sensory Area in Man.—Evans,[16] on the basis of a carefully studied series of cortical extirpations for scar, described sensory changes from lesions entirely confined to the posterior parietal lobules. The region of the supramarginal and angular gyri was found to

15. Such observations as these raise the question of what is meant by "dissociation of sensation." Separate cortical localization of the various modalities of sensation has been claimed on the basis of "dissociations" from cortical lesions. It is generally agreed that some anatomic separateness of neural substrate is the most frequent basis for dissociation, but there are probably many others. A dissociation produced by a cortical lesion does not necessarily mean a separate cortical representation; it may also mean that one function is more corticalized than the other, or is bilaterally represented, etc. "Double dissociation" must be demonstrated in order to establish a separate cortical localization of sense modalities. Moreover, any intermodality comparison is subject to errors from many sources and probably can be made only on the basis of quantitative data treated by psychophysical processes. The fantastic discrepanicies between the various proposed localizations of different modalities of sensation is sufficient evidence that the whole subject needs reconsideration.

16. Evans, J. P.: A Study of the Sensory Defects Resulting from Excision of Cerebral Substance in Humans, A. Research Nerv. & Ment. Dis., Proc. **15**: 331-366, 1935.

be particularly productive of sensory disturbances. The lesions in the postcentral gyrus, mostly small in the inferosuperior dimension, were accompanied by slight or no sensory symptoms. Of the four cases we have studied, only case 1 can be considered a truly critical test of Evans' views. In this case it was normal cortical tissue that was ablated, and no sensory symptoms were observed in neurologic examination before operation. The lesion in the parietal lobe was wedge shaped, with the point directed forward, and involved the inferior part of the superior lobule and the superior part of the inferior lobule; the postcentral gyrus was entirely unaffected. The existence of pronounced sensory symptoms in this case we consider to be strong confirmatory evidence of Evans' contention that lesions sparing the postcentral gyrus are productive of sensory disturbance and that the postero-inferior region of the parietal lobe is of particular significance to sensory functions.

Case 3, in which the cortical damage was predominantly anterior in the parietal lobe, and case 4, in which it was predominantly posterior (fig. 7), are of less localizing value because the critical boundary is somewhat uncertain in each case. Yet it is significant that in both sensory deficiencies were exhibited and in neither was the disturbance quantitatively great. In case 3 the possible damage to the postero-inferior parietal region must have been small, and yet the sensory deficit was similar to that in our first case, in which the lesion was restricted to that region. This suggests that if enough of the vertical extent of the representation of the arm in the postcentral gyrus is involved sensory symptoms result.

Effect of Training on Recovery.—A striking feature of the observations on the chimpanzee was the degree to which disturbances in discrimination of weight and roughness were subject to recovery. In this recovery two factors are involved: lapse of time after operation [17] and retraining.

The efficacy of retraining in promoting recovery is shown by an analysis of daily scores, which demonstrates that great improvement may occur within a training series, often between consecutive days and even within the daily training session. Improvement within a training series is shown in figures 2 *A* and 3 *B*. Such recovery therefore must be specific to the training situation. If a threshold series is conducted so that the weight difference is reduced after two training periods on each difference, the percentage of successful discriminations in the second period is consistently greater than in the first. It is as though each successively smaller weight difference presents a new problem to the animal

17. Lapse of time cannot, of course, be an active cause of recovery. Lapse of time allows for reeducation from ordinary cage activities and for possible internal factors positively related to time.

that requires relearning. This suggests that the recovery or relearning is quite specific, perhaps specific to the actual weight difference employed. Numerous repetitions of the same act, the unvarying and uncomplicated nature of the stimuli and the constancy of the sensory environment all undoubtedly favor recovery. Certain observations suggest that a much greater deficit is exhibited by the animals in a less stable situation.

It is a matter of considerable importance that the "plasticity" of the brain implied by the recovery in the chimpanzee experiments is not peculiar to the infrahuman primates. It was frequently encountered in the observations on clinical subjects. If a patient with a parietal lesion is asked to discriminate two grades of emery paper forty times, the errors in successive groups of ten trials may run 4, 2, 0, 0. When the difference in grade of emery paper is decreased, the number of errors

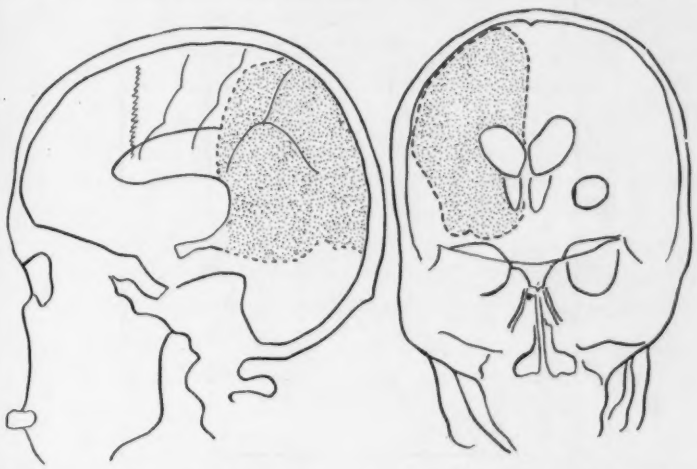

Fig. 7. (case 4).—Composite picture of the distribution of the contrast medium in the case of porencephaly, on which figure 5 *B* is based. The central fissure and the precentral and postcentral fissures were projected onto the encephalogram, on the basis of the average normal craniocerebral relationship.

increases, again to fall to the neighborhood of zero. Clearly, in this case the phenomenon is not any general "warming-up" effect. If the patient is tested day after day, there is often an upward creep in the level of performance. This is shown in figure 8 for the discrimination of roughness. In short, in clinical cases we have observed both the short term and the long term improvement with practice that characterizes the chimpanzee experiments. It goes without saying that such recovery increases the labor of obtaining stable thresholds in experiments on both animals and man.

The observations on chimpanzees and those on clinical subjects are in essential agreement with respect to the role of the parietal lobe in

sensory discrimination. In both the striking thing is that relatively large areas of the parietal cortex may be damaged without greatly disturbing the discrimination of roughness or lifted weights. The resulting disturbance is greatly lessened (man) or even abolished (chimpanzee) by retraining. In no sense does anesthesia result. This is not the behavior of a function which is focally localized in the cortex. The experiments indicate that both the postcentral gyrus and the posterior parietal lobule are concerned in the functions in question, but it is clear that neither is the site of a focal representation. Since parietal lobectomy in the chimpanzee does not completely abolish the ability to perform sensory discriminations, the areas of the cortex subserving such discriminations must extend beyond the parietal lobe of one hemisphere. The regions

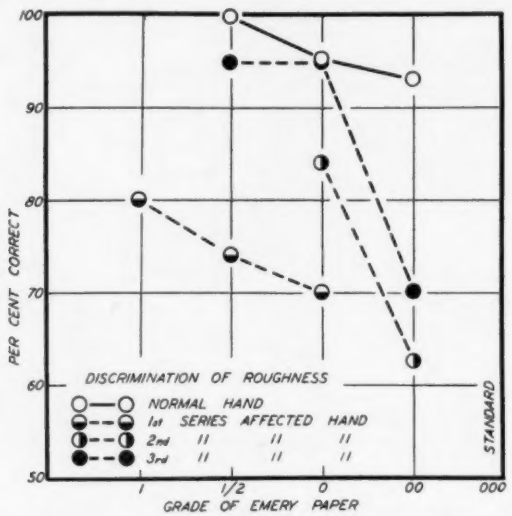

Fig. 8 (case 3).—Discrimination of emery paper. This graph illustrates the progressive improvement in discrimination as a result of practice. The deficiency of the affected hand persists after training for only the finest discrimination (OO versus OOO).

responsible for recovery of function may be one or all of the following: (1) motor areas, (2) the opposite parietal cortex and (3) the thalamus.

There is a clear difference in degree between the effects of partial lesions of the parietal cortex in man and those in the chimpanzee. In the latter, the alterations in discriminatory ability which occur are not permanent and largely disappear with retraining. In man, smaller lesions result in disturbances which are permanent. The residual deficit in some cases, however, is slight (cases 3 and 4). The difference between man and the chimpanzee with respect to the sensory functions studied is, then, one of degree, i. e., the degree of corticalization. Similarly, these func-

tions are more corticalized in the chimpanzee than in the monkey. In all three phylogenetic stages somatic sensory function, with respect both to the degree of corticalization [18] and to the concentration of representation in the cortex, is less far advanced than that seen in the visual system.

CONCLUSIONS

Parallel studies of the cortical localization for discrimination of rougness and of lifted weights in monkey, chimpanzee and man lead to the following conclusions:

1. A progressive corticalization of sensory functions is reflected in the disturbances of sensory discrimination following lesions of the postcentral gyrus and the posterior parietal lobules. When tests are made several weeks after operation, these lesions in the monkey are without effect on weight-discriminatory ability; in the chimpanzee the disturbances that occur disappear with retraining; in man marked blunting of weight-discriminatory ability is reduced by training to a small, but definite, permanent deficit.

2. An extensive parietal lesion in man induces a relatively small permanent deficit in the ability to discriminate weight and roughness. It is inferred from several lines of evidence that these functions are represented widely throughout the parietal lobe. In the chimpanzee the whole parietal lobe appears to be involved, and tissue outside the parietal lobe (of one hemisphere) can sustain some degree of discrimination.

3. In man and the chimpanzee damage to the posterior parietal lobules of the parietal lobe (sparing the "primary" sensory area of the postcentral gyrus) reduces ability to discriminate weight and roughness. This was true in one case after fairly restricted excision of a region in the neighborhood of the angular and supramarginal gyri.

4. The degree of recovery of discriminatory ability possible after partial lesions of the parietal lobe is a striking feature of the observations on both the chimpanzee and man. Retraining is an important factor in this recovery. Several facts suggest that the postoperative improvement manifested during retraining is specific to the particular testing situation, and it is inferred that the basis of the improvement lies in increased evaluation of residual cues.

ABSTRACT OF DISCUSSION

DR. JOSEPH P. EVANS, Montreal, Canada: I find that it is difficult to give a well considered discussion of this paper because, owing to a series of events over which the authors and I had no control, Dr. Ruch's reading of it has been in the nature of an introduction. It seems to me that the study is of great importance,

18. Marquis, D. G.: Phylogenetic Interpretation of the Functions of the Visual Cortex, Arch. Neurol. & Psychiat. **33**:807-815 (April) 1935.

because it is the third of three detailed attempts to localize accurately the modalities concerned with cortical sensation.

The first was that of Head and Holmes, in which they employed excellent methods but were handicapped by the fact that they had to judge the localization of the lesions in their patients by external marks left by the gunshot wounds.

In a second detailed study, which was carried out in Montreal, it was possible to localize accurately the areas of substance that were removed; the third paper, however, presents methods which can be applied clinically, and these detailed psychologic and neurologic methods combined with more accurate localization will help to fill the gaps so far as knowledge of human cerebral localization is concerned.

The deficiencies of the method from the standpoint of clinical neurology are obvious to the authors. They call attention to this fact. Nevertheless, the method has much to recommend it.

I wish to ask one question. I was not clear about the postoperative improvement in the discrimination of weight. In our human material, my associates and I found that there was a definite period when cortical sensory function might be disturbed completely but that by the end of thirty-five days, usually, any cortical dysfunction from which the patient would recover had disappeared. I wonder whether in the present series of animals the time limit was such that the improvement was dependent on recovery from diaschisis.

Dr. Israel S. Wechsler: I, too, have little to add to this paper. It seems to me that it is an excellent way of demonstrating in the animal many of the facts that are known to exist in man. How applicable animal experimentation of this kind is to man it is difficult to say. It is of interest that there can be a great deal of recovery in the animal. This is also true in man, although if the stereognostic sense is lost, the damage is apt to be permanent. Naturally, this depends on the extent and duration of the process.

Dr. Theodore C. Ruch, New Haven, Conn.: In answer to the question of Dr. Evans, it should be said that retraining was deliberately postponed until several weeks after operation to avoid diaschisis. The recovery with retraining occurs with a suddenness that means that not recovery from diaschisis but the actual retraining received in the course of testing is the important factor.

As to whether the stereognostic sense is subject to recovery: The animal experiments show that it is. A chimpanzee has been trained to discriminate a pyramid and a cone and a pyramid and a wedge. After operation both habits are lost. With retraining the animal can discriminate a cone and a pyramid—an easy discrimination. It fails entirely, and restraining does not make it able, to discriminate a pyramid and a wedge. Not only is stereognosis not a "sense" (it is a higher perceptual level based on sensation) but it is not a unitary thing; it is rather a series of processes of varying complexity. I believe that if stereognosis is studied at several levels of complexity, it will be found that the loss of stereognostic ability in many cases of parietal lesion is only partial and is subject to a certain degree of recovery. This, of course, does not mean that recovery will bring the ability back to normal.

DYSTONIA MUSCULORUM DEFORMANS

A CLINICOPATHOLOGIC STUDY

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AND
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Dystonia musculorum deformans, or torsion dystonia, originally was regarded as hysteria by Schwalbe.[1] Ziehen [2] described a case, calling the disorder spasm neurosis. Oppenheim,[3] who added four cases, was the first to consider the disease organic. Mendell,[4] without histopathologic proof, postulated possible lesions in the lenticular nucleus and brachium conjunctivum. The histopathologic reports in a few instances added little to the exact understanding of the disorder. The confusion arose mainly because of the difficulty in differentiating this condition from other dyskinesias, such as progressive hepatolenticular degeneration and chorea. Some observers have been inclined to consider dystonia musculorum deformans as a variant of hepatolenticular degeneration rather than as a disease entity. The constant histopathologic changes in the striatum and the dentate nucleus in our four cases, in which the patients were observed clinically for several years, may throw some light on the understanding of this disease.

REPORT OF CASES

CASE 1.—M. S., a girl aged 12 years, who was born in the United States, was admitted to the Montefiore Hospital on Aug. 18, 1935. The father was born in Russia, and the mother, in Poland; there was no kinship. A familial history

From the Neurological Division and the Neuropathological Laboratory, the Montefiore Hospital.

Read at the Sixty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1937.

1. Schwalbe, M. W.: Eine eigentümliche tonische Krampform mit hysterischen Symptomen, Inaug. Dissert., Berlin, G. Schade, 1908.

2. Ziehen, T.: Fall von tonischer Torsionsneurose, Neurol. Centralbl. **3**:109, 1911.

3. Oppenheim, H.: Ueber eine eigenartige Krampfkrankheit des kindlichen und jugendlichen Alters (Dysbasia lordotica progressiva, dystonia musculorum deformans), Neurol. Centralbl. **30**:309, 1911.

4. Mendell, K.: Torsiondystonie, Monatschr. f. Psychiat. u. Neurol. **46**: 309, 1919.

of mental or nervous disorder was not present. A sister and brother were alive and well. At 6 weeks of age the patient contracted whooping cough, accompanied by attacks of paroxysmal respiratory dyspnea and cyanosis, almost to the point of asphyxia. After the first paroxysm the mother noticed that the child had a "vacant stare" and that the right upper extremity was held in posterolateral extension and rotated inward, with the palm upward. She recovered completely and remained well until the age of 2½. Because of mental retardation, craniotomy was performed at this time. After this she was unable to sit up. From the third to the sixth year she was bedridden but was able to eat, to use the extremities and to speak. At the age of 6 muscular pain in the lower extremities and the lumbar region prevented the child from lying flat on her back. The lower extremities were flexed. Any attempt to extend them caused severe pain. At this time there appeared athetoid movements of the right hand and massive swinging movements of the right upper limb. The patient could overcome these by placing her hand behind her back. Two years before admission, at the age of 10, the right lower extremity became rotated inward, with flexion at the hip and knee.

Physical Examination.—The child was undernourished. There were: a high-arched palate; receding mandible; marked asymmetry of the chest, the left breast being larger than the right, and lordosis and scoliosis to the left. The liver and spleen were not enlarged.

Neurologic Examination.—The patient was unable to walk; she lay in bed with the right arm and right leg in marked flexion, the left arm alternately flexed and extended (fig. 1) and the left leg in extension. There were marked dystonic movements of practically all muscle groups, slight facial grimacing when at rest and athetoid movements of the fingers and toes. Dystonic movements increased on voluntary effort. Muscular tonus alternated between hypotonia and hypertonia. The muscles appeared wasted; there were no fibrillations. The deep reflexes could not be elicited on the right because of the marked muscle spasm; there were no other pathologic reflexes or sensory disturbances. There was facial asymmetry. The patient was dysarthric but not aphasic. Spasmodic torticollis and hypertrophy of the left sternocleidomastoid muscle were present (fig. 1). Otherwise the cranial nerves were normal in function. The patient's education was limited, but she appeared of average intelligence. Inability to write was due to the dystonic movements.

Course.—Craniotomy and excision of the right premotor cortex were performed on June 30, 1936, for relief from the dystonic phenomena. The patient's condition remained unchanged after operation. Because of restlessness, she received phenobarbital, and occasionally chloral hydrate. For about a year before she died she received 0.45 grain (0.29 Gm.) of codeine once or twice a day, and for the last two months, morphine sulfate, in 0.008 Gm. doses, once or twice a day. She died suddenly on Jan. 13, 1937.

Laboratory Data.—Studies of the blood and spinal fluid gave normal results.

Autopsy.—Except for the muscles, the organs showed no outstanding gross or microscopic changes. The muscle fibers had a homogeneous pale, glassy appearance and showed loss of striations. Areas of fibrosis and increase in the nuclei of the sarcolemma were also seen.

Brain: The brain, which was removed four hours after death, weighed 1,180 Gm. and showed a postoperative scar at the site of excision of the middle and foot of the right premotor area. There were dilatation of the lateral ventricles and marked shrinkage of the basal ganglia. Sections from various cortical con-

volutions and the basal ganglia, mesencephalon, cerebellum, dentate nuclei, brain stem and spinal cord were embedded in celloidin (pyroxylin) and stained by the myelin sheath and cresyl violet methods. Sections from the basal ganglia and the dentate nuclei were fixed in 95 per cent alcohol and stained by the cresyl violet and Turnbull blue methods. Sections from the basal ganglia were frozen and stained by the myelin sheath, Bielschowsky, Holzer, sudan III, Cajal gold sublimate and microglia methods. Sections of the spinal cord were fixed in Müller's fluid and stained by the Marchi method.

Microscopic Examination of Brain.—Cerebral Convolutions: Sections of the right premotor area disclosed distortion in the arrangement of the cyto-architectural layers (fig. 2*A*). Many of these layers were destroyed and replaced by glial tissue (microglia cells and astrocytes) and proliferated vessels (fig. 2*A*).

Fig. 1 (case 1).—Photograph showing dystonic features of the muscles of the face and neck, flexion of the right upper and both lower extremities and extension of the left upper extremity. Note the left striatal foot and contractures.

The few remaining islands of nerve cells showed various pathologic changes, such as coagulation necrosis, ischemia, chromatolysis and neuronophagia; some looked like fantom cells. In many areas the nerve cells were totally replaced by glial tissue. Other sections from both hemispheres, near and distant from the operative field, showed thinning and moderate distortion in the arrangement of the cyto-architectural layers (fig. 2*B*). The cortical vessels were increased in number, and the endothelial layer was proliferated. The ganglion cells of the various layers showed all types of destruction: ischemia, chromatolysis and complete disintegration. The pathologic process was most pronounced in the frontal, premotor, motor, insular, superior parietal, angular and supramarginal gyri (fig. 2*A* and *B*).

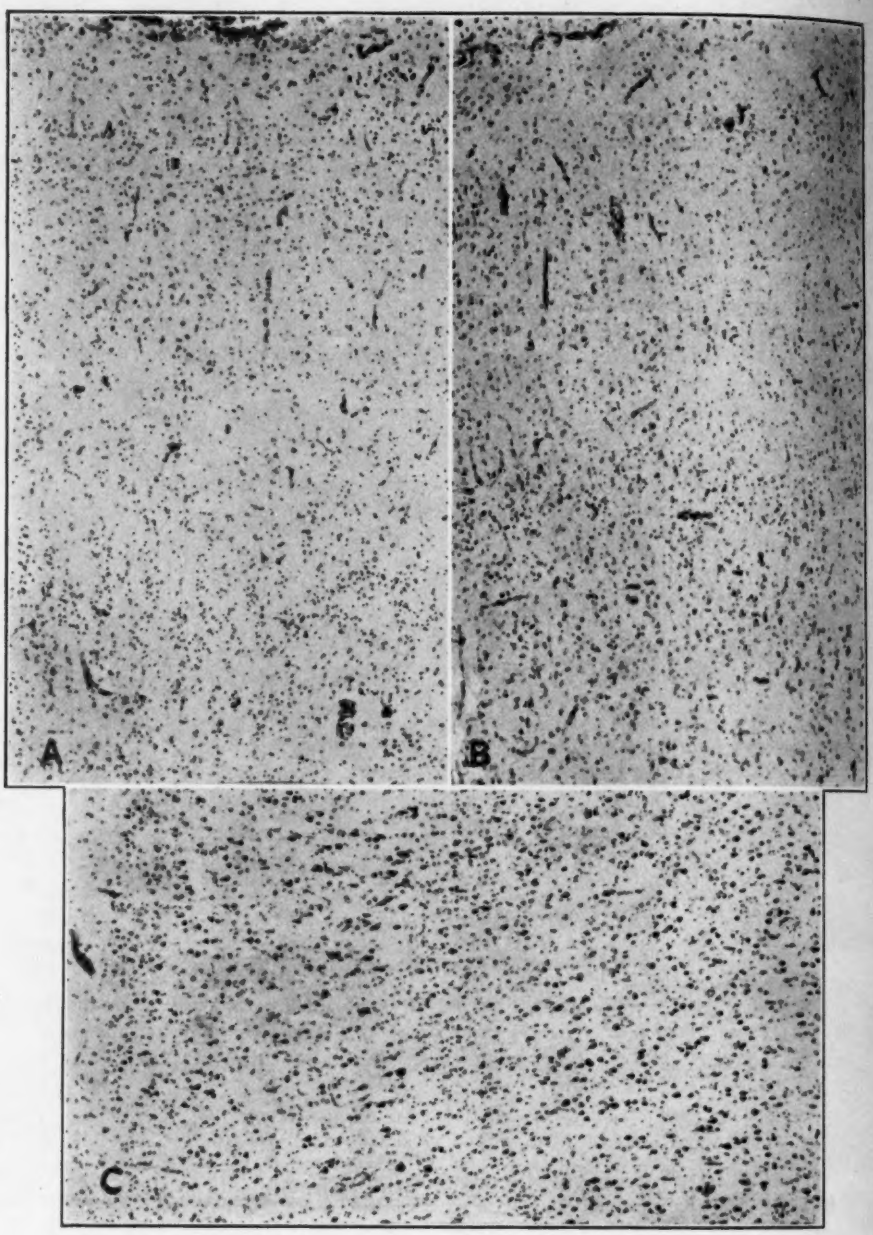

Fig. 2 (case 1).—*A*, premotor area (area 6), showing distortion in arrangement of the cyto-architectural layers, proliferation of the cortical vessels and dropping out of nerve cells; × 30. *B*, supramarginal gyrus, with distortion in arrangement of the cyto-architectural layers, proliferation of the cortical vessels, most marked in the first three layers, and dropping out of nerve cells. These changes may be compared with the normal, shown in *C*; × 30. *C*, normal supramarginal gyrus; × 30. Cresyl violet stain.

Basal Ganglia: The lateral ventricles were dilated. The anterior third of the striatum disclosed marked shrinkage of the caudate nucleus and putamen (fig. 3*A*). The caudate nucleus was reduced to about one-half its size; the putamen, to about one-fourth. The striatal areas near the internal capsule stained darkly. The myelin fibers in these darkly stained areas were arranged in close bundles; some were slightly disintegrated. In Holzer preparations the caudate nucleus and putamen stained deeply and had the appearance characteristic of status fibrosus

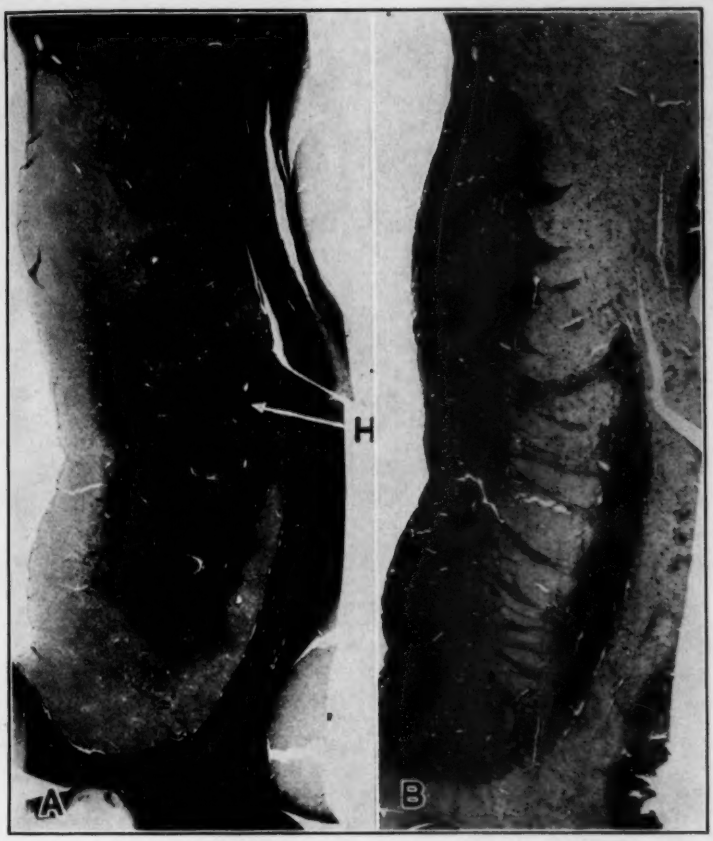

Fig. 3 (case 1).—*A*, marked shrinkage of the caudate nucleus and putamen. The latter is reduced to about one-fifth the normal size and shows marked status fibrosus and hypermyelination (*H*); myelin sheath stain. *B*, an area similar to that shown in *A*, with extensive gliosis of the caudate and putamen; Holzer stain.

(fig. 3*B*); they contained numerous glia cells and glia fibers. In sudan III preparations a few perivascular spaces were filled with fat. In the Bielschowsky, Cajal and microglia preparations there were occasional breaking down of axis-cylinders, swollen oligodendroglia cells and proliferation of the microglia cells and astrocytes and of the vessels. In cresyl violet preparations the large and small ganglion cells of the striatum were diminished in number. Some of the large ganglion cells

had a washed-out appearance, and their nuclei were displaced to the periphery; others were completely disintegrated or showed ischemic cell changes (fig. 4). Proliferation of vessels and increase in glia cells were present in the caudate nucleus and putamen (fig. 5).

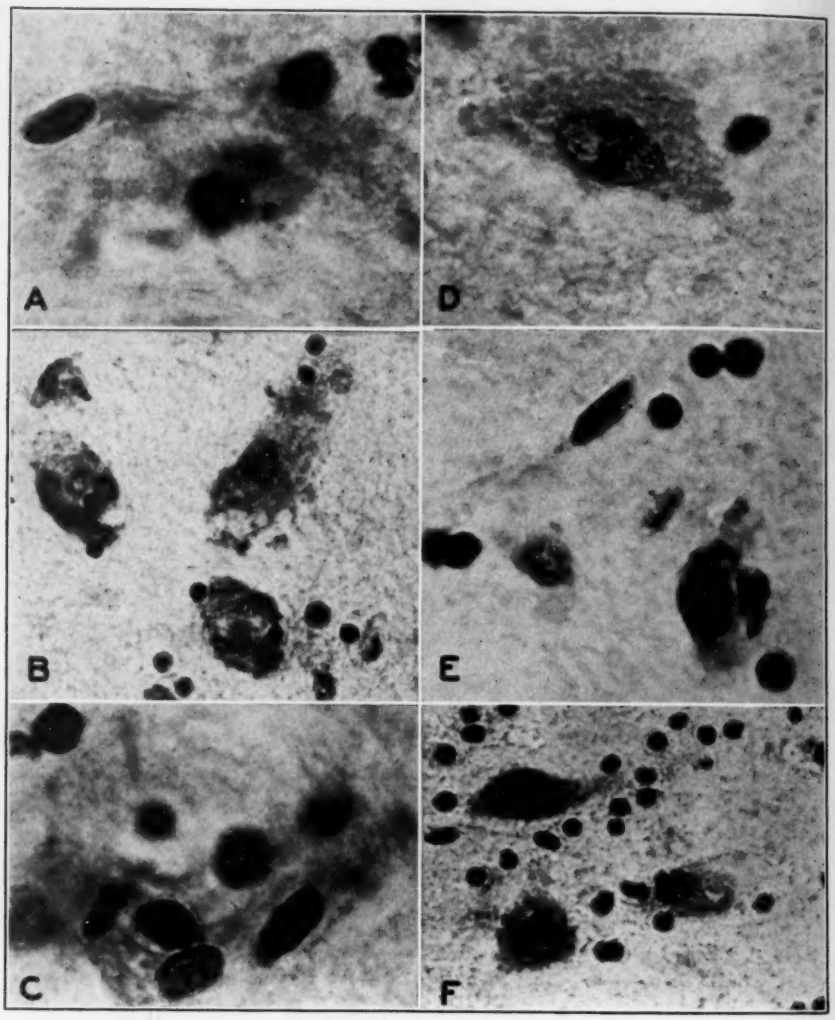

Fig. 4 (case 1).—*A*, disintegrated large ganglion cell of the striatum; × 800. *B*, severe cell changes in the striatal nerve cells; × 400. *C*, neuronophagia and marked destruction of the large nerve cells of the putamen; × 800. *D*, large, pale nerve cell of the striatum, with the nucleus displaced to the periphery; × 800. *E*, ischemic nerve cell of the putamen and rod-shaped microglia cell; × 400. *F*, ischemic cell changes in the corpus Luysi; × 400. Cresyl violet stain.

In sections through the beginning of the left globus pallidus there were shrinkage of the caudate nucleus and putamen, pallor of the caudate nucleus, status fibrosus of the upper half of the putamen and status marmoratus of the lower

half (fig. 6*A*). The caudate nucleus showed poverty of nerve fibers. In the area of status fibrosus there were closely packed bundles of myelin, some of which were disintegrated. In the area of status marmoratus a network of islands of myelin encircled pale islands of nerve tissue (fig. 6*A*). Delicate, poorly stained myelin sheaths running in various directions and exceeding the number of axis-cylinders were also noted. Cresyl violet preparations showed changes similar to those in the previous sections.

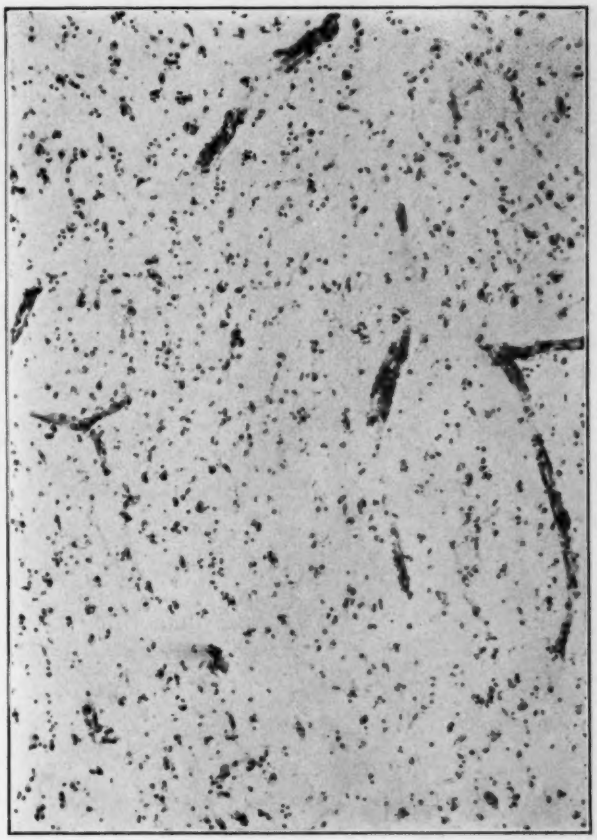

Fig. 5 (case 1).—Proliferation of the vessels and increase in glia cells of the striatum; × 70. Cresyl violet stain.

In sections passing through the right thalamic nuclei there were pallor of the caudate nucleus and shrinkage of the putamen, with status fibrosus of its upper three fourths and status demyelinisatus of its lower fourth (fig. 6*B*). The globus pallidus was atrophied, and its inner segment stained poorly, as in status dysmyelinisatus (fig. 6*B*); the pallidal nerve fibers of the inner segment were slightly disintegrated. The pallidal nerve cells were small and closely packed together and showed marked ischemic changes, as did the nerve cells of the claustrum. In sections through the left thalamic nuclei and the beginning of the

substantia nigra there were status dysmyelinisatus of the caudate nucleus, putamen and pallidum and marked thinning of the various pallidal laminae and of the ansa lenticularis (fig. 7). The microscopic changes were similar to those in previous sections.

Examination of sections through the substantia nigra and red nucleus revealed only ischemic changes in some of the nerve cells of the right corpus Luysi (fig. 4 *F*).

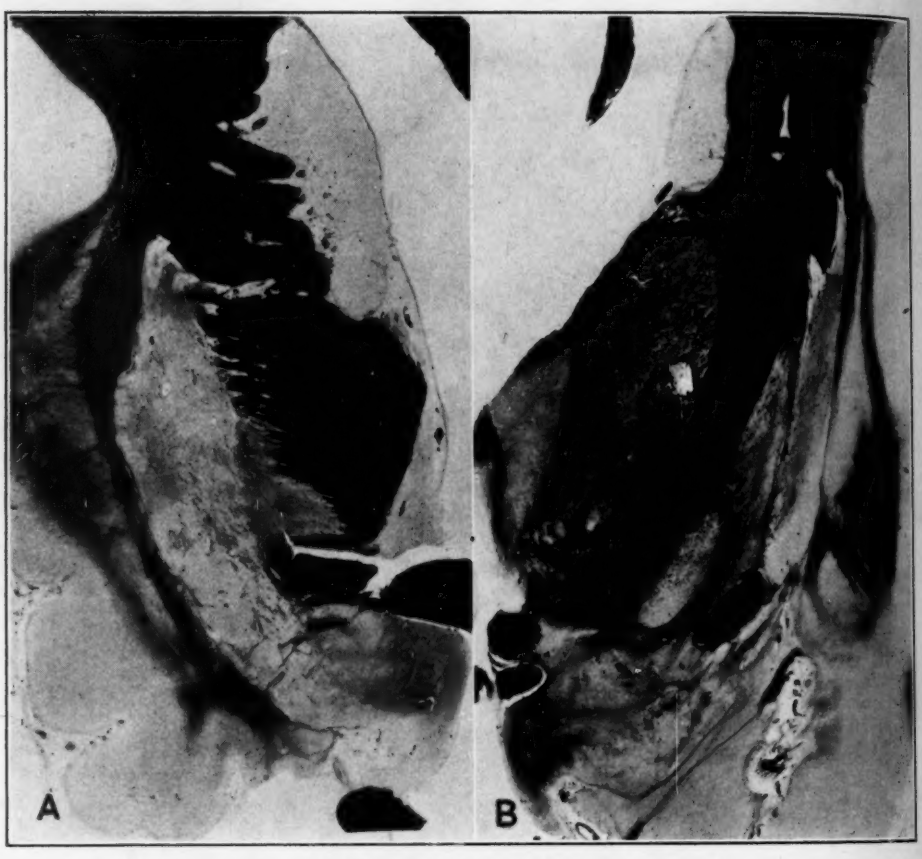

Fig. 6 (case 1).—*A*, shrinkage of the left striatum, status marmoratus of the lower two thirds of the putamen and of the claustrum and external capsule and status dysmyelinisatus of the caudate nucleus and pallidum. *B*, shrinkage of the right striatum and pallidum and status dysmyelinisatus of the caudate nucleus, part of the putamen, claustrum and inner segment of the pallidum. Myelin sheath stain.

Cerebellum and Dentate Nuclei: The cerebellum appeared normal. In the dentate nuclei there were marked ischemia of the nerve cells, chromatolysis and increase in glia cells (fig. 8 *B*).

Brain Stem: The medulla oblongata was shrunken and appeared much smaller than normal. Some leaflets of the inferior olivary nuclei showed marked ischemia of the nerve cells and slight gliosis (fig. 8*C*). The corpus restiforme was slightly reduced on both sides.

Spinal Cord: No abnormalities were detected.

The posture and the involuntary movements were typical of dystonia. The slight facial grimacing, the athetoid movements and the dysarthria,

Fig. 7.—Section through the left thalamic nuclei, showing status dysmyelinisatus of the caudate nucleus, putamen and pallidum and marked thinning of the pallidal laminae and of the ansa lenticularis. Myelin sheath stain.

although occasionally described, are less frequently seen in this disorder. The paralysis of one limb and the general retardation in physical development following whooping cough suggested the possibility that this disease of childhood was an etiologic factor. Histopathologically, inflammation or hemorrhages, the usual complications of pertussis, were not observed in the nervous system. This is the only case in our series

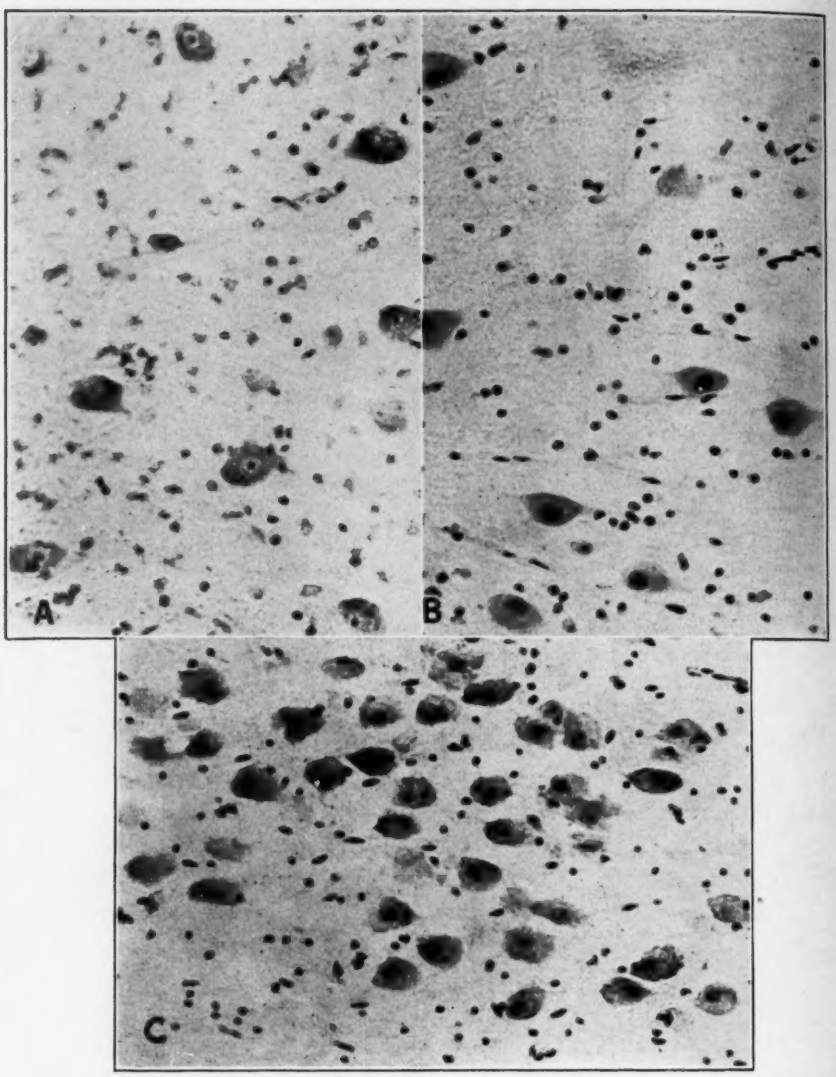

Fig. 8 (case 1).—*A*, normal nerve cells of the dentate nucleus; × 200. *B*, ischemic cell changes in the nerve cells and increase in the glia cells of the dentate nucleus; × 200. *C*, ischemic nerve cell changes in the inferior olivary nuclei; × 200. Cresyl violet stain.

in which there was extensive involvement of the cortical convolutions, claustrum and inferior olivary nuclei. We are not certain whether the slight changes in some of the nerve cells of the right corpus Luysi were responsible for the hemiballistic type of movements.

CASE 2.—R. C.,[5] a girl aged 17, was admitted to the Montefiore Hospital on Jan. 20, 1920. The parents and the patient were born in Russia. There was no consanguinity of the parents and no familial history of mental or nervous disorder. Three sisters and a brother are alive and well. The past history was without significance.

In the summer of 1917, while in the country, the patient was frightened by a thunder storm. Immediately after, there appeared jerky movements in all parts of the body, most marked in the hands, legs, shoulders and face. These movements were aggravated by the least excitement. Neurologic examination at that time gave normal results except for the involuntary movements. The diagnosis was major hysteria. Various and intensive psychotherapeutic methods, such as hypnosis and psychoanalysis, were unsuccessful. In April 1924 the patient became obstinately constipated for a week and vomited for two days; enemas and cathartics were of no avail. Two months later she had a similar attack of constipation, with cramplike abdominal and suprapubic pains and retention of urine. She was catheterized two or three times daily for about six months. On several occasions outbursts of crying and shouting were followed by lethargy, which lasted two days or longer. It was difficult to arouse her from this state.

Physical Examination.—The patient was well nourished, with protuberance and distention of the abdomen. The liver and spleen were not enlarged. Scoliosis of the spine was present.

Neurologic Examination.—There were twitchings of the left angle of the mouth, irregular movements of the tongue and hyperextension of the left upper extremity at the elbow and, at times, at the wrist, with eversion. There was an interplay of hypotonia and hypertonia of the various muscle groups of the extremities. The right shoulder was at times the seat of rhythmic ticlike movements which were influenced by attention and emotion. During the patient's first hospitalization she exhibited movements which were then regarded as of purely functional nature and later, in retrospect, as of striatal origin. Likewise, the vermiform movements in the muscle groups of the lower extremities were undoubtedly dystonic. These movements were best revealed by an analytic study with the slow motion picture camera. The lower extremities were flexed at the hips and knees; the feet were extended and inverted, and the toes flexed, simulating a striatal foot (fig. 9*A*). There was wasting of the muscles of the lower extremities, but no fibrillations. The dyskinetic form of dystonia was replaced by the myostatic form, with contractures (fig. 9*B*) of varying degrees, which, by manipulation, could be temporarily overcome. Function of the cranial nerves was normal. At times the patient had episodes of emotional instability.

Course.—In July 1924 there developed acute cystitis, pyelitis and pyelonephritis, from which the patient recovered in a few weeks. In October 1924 bilateral involuntary winking movements were noted. Frequent gastrointestinal attacks

5. This patient was demonstrated by one of us (Goodhart) in motion pictures at various European clinics in 1925. The opinions of leading European neurologists varied as to whether the disease was entirely of psychogenic or of organic nature.

occurred. Any emotional upset increased the heart rate to between 100 and 180 beats per minute. Paroxysms of dyspnea, which were characterized by choking and inspiratory distress lasting from thirty to sixty seconds, were noted. Another gastrointestinal upset was accompanied by urethral spasm, retention of urine and dribbling. Administration of atropine and scopolamine—parasympathetic depressants—excited vomiting, retching and retention of urine. The use of physostigmine and pilocarpine—parasympathetic stimulants—released slightly the pyloric spasm and influenced favorably the vomiting.

Between 1928 and 1931 several intermittent infections developed, such as bronchopneumonia, mastitis of the right breast and pleurisy on the left side of the chest. In 1932 the head was turned markedly to the left, and the right sternocleidomastoid muscle stood out prominently. In September 1935 neuritis of the right foot and both hands developed, owing to avitaminosis induced by the persistent vomiting; with forced nourishment this disappeared. In August 1936 there

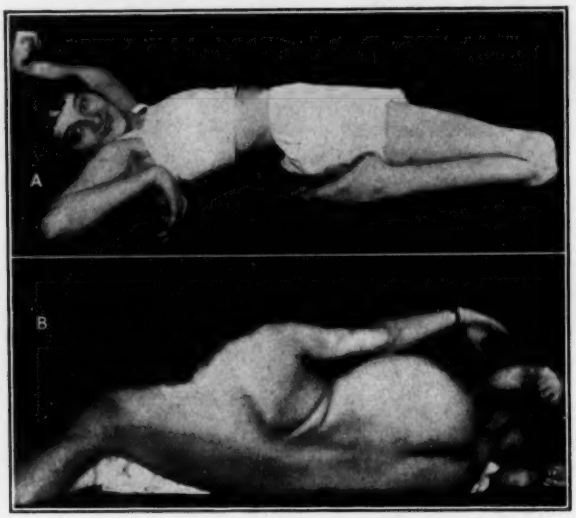

Fig. 9 (case 2).—*A*, flexion of the lower extremities, extension of the left upper extremity and flexion of the right upper extremity at the elbow and wrist. *B*, scoliosis, striatal foot and contractures of the lower extremities.

appeared marked dysarthria and another attack of peripheral neuritis, consisting of paralysis of the right leg with foot drop, absence of the ankle jerk and loss of sensory appreciation, of the glove and stocking type. The patient died Jan. 3, 1937, of bronchopneumonia.

Laboratory Data.—The average blood pressure was 130 systolic and 80 diastolic. Examination of the blood revealed slight secondary anemia. Blood chemistry studies and Wassermann tests with the blood revealed no abnormalities. The urine, except during the cystitis, was not abnormal. Roentgen examination disclosed scoliosis of the lumbar portion of the spine, with convexity to the left. Fluoroscopic examination of the gastrointestinal tract showed regurgitation of some of the barium following its entrance into the stomach and, on one occasion, reversal of peristalsis. The stomach was of "steer horn" type and hypertonic;

at times, because of the violent contractions, it had an hour-glass appearance. One-half hour after the meal little barium had left the stomach; the duodenal cap was not visualized.

Autopsy.—The general gross and microscopic diagnoses were: bronchopneumonia, cystitis and abscess of the left thigh.

Brain: The brain, which was removed two hours after death, weighed 1,240 Gm. Coronal sections were cut. Except for slight shrinkage of the right caudate

Fig. 10 (case 2).—Pallor of the caudate nucleus; status marmoratus of the putamen, especially of its outer, middle and lower surfaces, and pallor of the pallidum. Myelin sheath stain.

nucleus and pallor of the putamen, no gross abnormalities were seen. Sections were taken from areas similar to those in case 1 and were studied by the same methods.

Microscopic Examination.—Cerebral Convolutions: No changes were noted in the various convolutions, except a slight accumulation of Alzheimer glia cells, of type II, in the superior parietal region.

Basal Ganglia: In sections through the anterior third of the striatum there were slight shrinkage and pallor of the caudate nucleus and status marmoratus of the upper pole of the putamen. In sections through the anterior segment of the globus pallidus there were slight shrinkage and status marmoratus of the upper, outer and lower parts of the putamen (fig. 10). With a higher power, slight disintegration of the myelin fibers of the putamen was seen, especially in

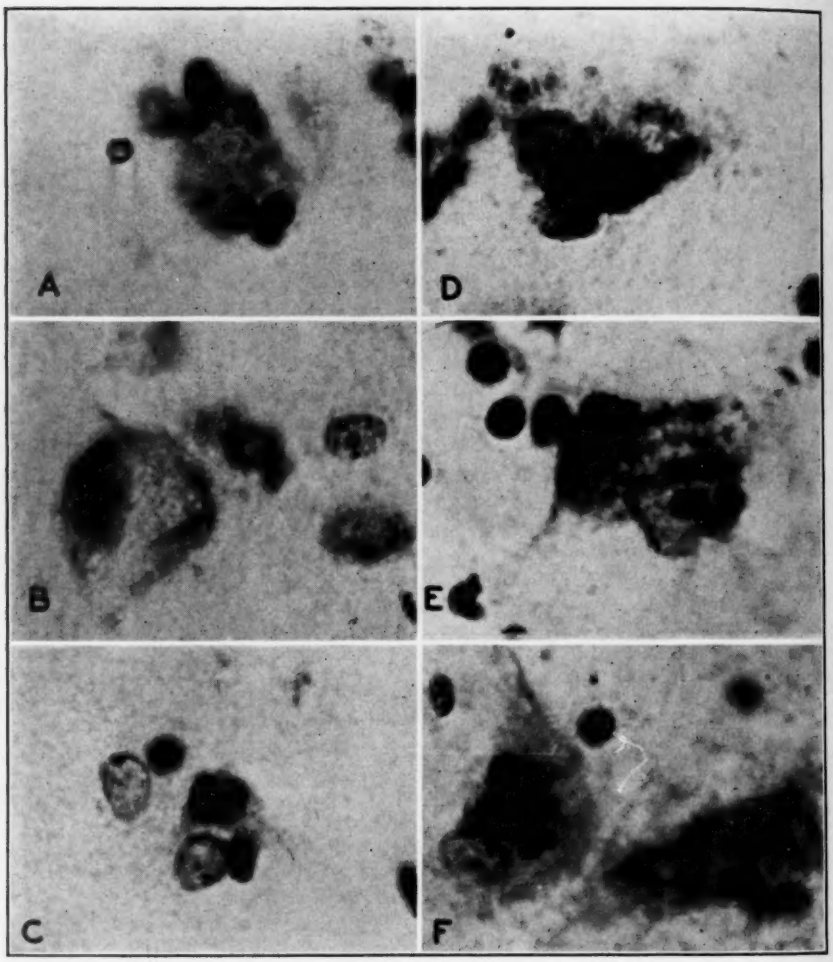

Fig. 11 (case 2).—Pathologic changes in the nerve cells of the striatum; × 800. *A*, neuronophagia; *B*, marked chromatolysis and peripherally displaced nucleus; *C*, small nerve cell of the caudate nucleus surrounded by two Alzheimer glia cells, of type II; *D*, disintegrated nerve cell of the putamen; *E*, disintegrated nerve cell of the putamen having the appearance of an Alzheimer glia cell, and *F*, two diseased nerve cells of the pallidum, one of which shows neuronophagia. Cresyl violet stain.

the area of the status marmoratus. The areas of status marmoratus contained pale islands of nerve tissue, encircled by a network of dark strands of myelin. The dark areas contained poorly stained myelin sheaths running in all directions. The pallidum was slightly pale (fig. 10), but the myelin sheaths were normal. In sudan III preparations fat was seen in the perivascular spaces of some vessels near the ependyma, in the caudate nucleus and in the internal capsule. In Holzer

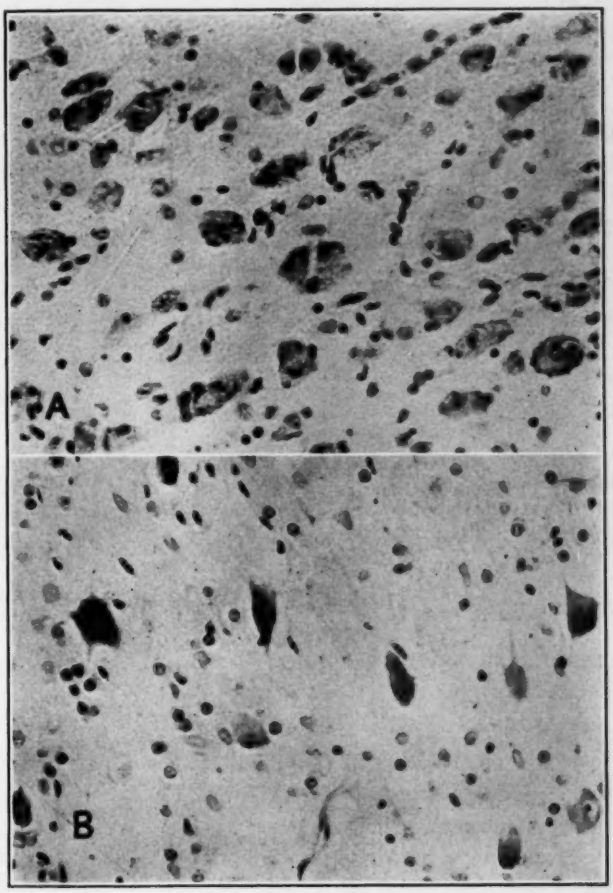

Fig. 12 (case 2).—*A*, diminution in pigment granules of the hypothalamic nerve cells (nucleus paraventricularis); × 200. *B*, pyknosis, chromatolysis of nerve cells of the dentate nucleus and increase in microglia (rod-shaped) cells; × 200. Cresyl violet stain.

preparations there was a slight increase in the glia nuclei. In Bielschowsky preparations occasional disintegrated axis-cylinders were seen. In caudal sections there were status dysmyelinisatus of the inner segment of the right globus pallidus only and thinning of the ansa lenticularis. With the Turnbull blue reaction deposits of iron were seen near some of the vessels and glia cells. In cresyl violet

preparations the large ganglion cells of the striatum were decreased in number and showed all types of pathologic changes: complete disintegration; loss of Nissl substance; peripherally displaced nuclei, and satellitosis (fig. 11). A few small nerve cells of the striatum showed ischemic cell changes. There was also an increase in the number and size of the microglia cells, many of which looked like rod cells. Alzheimer glia cells, of type II (fig. 11 *C*), were also seen. In some fields the disintegrated nerve cells appeared like Alzheimer glia cells of type I (fig. 11 *E*). The upper third of the putamen was more affected than the middle or the lower third. The vessels in the pallidum were calcified. The nerve cells in the inner segment of the right pallidum showed some loss of Nissl substance, with peripherally displaced nuclei, slight neuronophagia (fig. 11 *F*), Alzheimer glia cells of type II and an increase in microglia cells. The hypothalamic nerve cells showed marked loss in normal pigment (fig. 12 *A*). The nerve cells of the corpus Luysi, substantia nigra and red nucleus were normal.

Cerebellum and Dentate Nuclei: The structures of the cerebellum were normal. The nerve cells of the dentate nucleus showed chronic cell changes, chromatolysis and pigment atrophy (fig. 12 *B*); the glia nuclei were increased in number.

Brain Stem: There were no abnormalities in the pons or medulla oblongata.

Spinal Cord: In Marchi preparations there was a slight area of degeneration on the left side near Helweg's and the ventral spinocerebellar tract (fig. 13 *A*). This area consisted of disintegrated myelin and black granules (fig. 13 *B*). The same process was noted in the myelin sheath preparation (fig. 13 *B*).

In this, as in many similar cases, the dystonia at one time was considered to be hysteria major. The temporary recession of involuntary movements associated with dystonia, as occurred in this instance, is no indication of psychogenicity. In induced sleep or in hypnosis the dyskinesia may disappear almost entirely. We have had an opportunity to observe true cases of dystonia in which the dystonic movements ceased after hypnosis.

The vegetative disturbances, consisting of severe constipation, abdominal distention, nausea and vomiting, urinary disturbances, tachycardia and paroxysms of dyspnea, indicate that the visceral musculature may also become involved in cases of dystonia. The vomiting and inability to retain nourishment led on two occasions to avitaminosis and peripheral neuritis. The exacerbation of vomiting, retching and retention of urine after administration of atropine and scopolamine was thought to be due to parasympathetic depression or sympathetic overstimulation. The use of parasympathetic stimulants offered some relief.

In contrast to the other three cases in our series, the nerve cells in the dentate nuclei disclosed chronic, not ischemic, cell changes and chromatolysis. The area of degeneration in the left side of the cord near the ventral cerebellar tract did not correspond to the usual position of the extrapyramidal pathways. It is possible, however, that some of the extrapyramidal pathways in the spinal cord may have a different position than those ascribed to the rubrospinal tract. In the other cases of dystonia sections of the spinal cord stained by the same methods did not show pathologic changes in the corresponding areas.

Case 3.—J. L., a boy aged 11, who was born in the United States, was admitted to the Montefiore Hospital on Feb. 13, 1922. The parents, first cousins, were born in Russia. Three other children are living and well. There was no familial history of mental or nervous disorder. The past history of the patient was irrelevant. In 1919, at the age of 8 years, the left foot, and a year later the

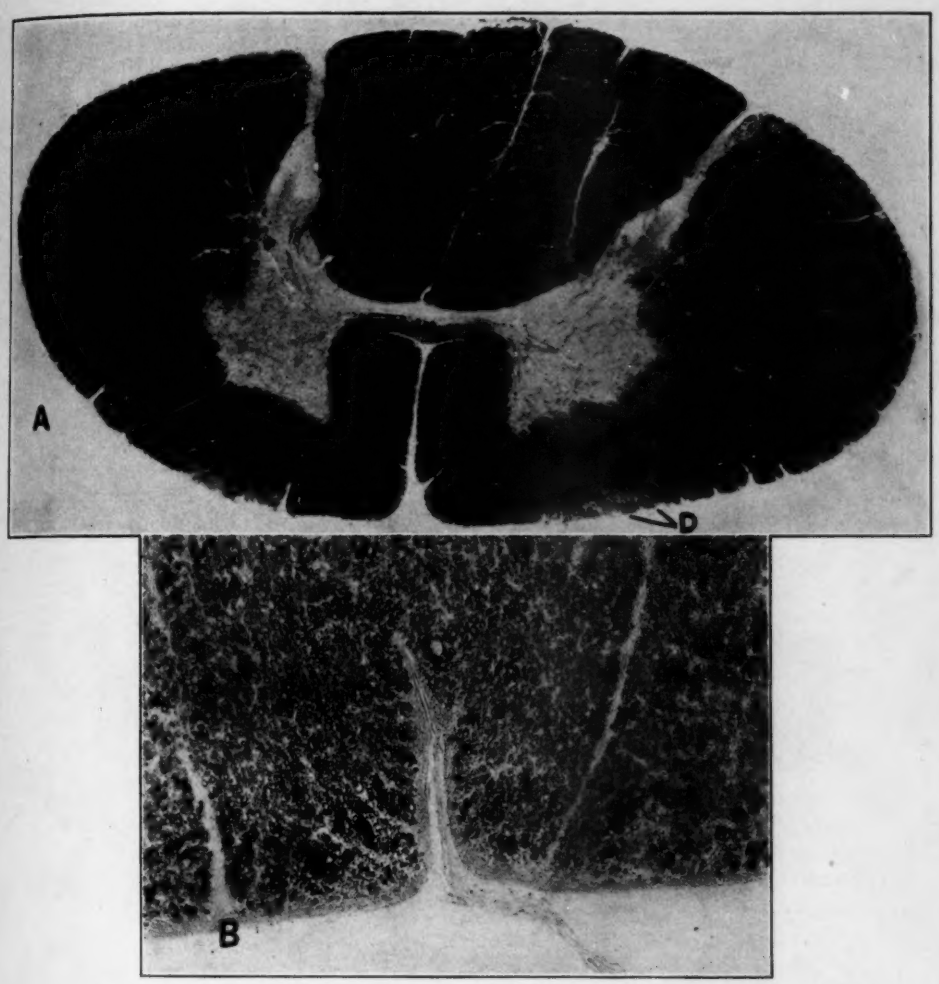

Fig. 13 (case 2).—*A*, degeneration (*D*) of myelin fibers of the spinal cord, near Helweg's tract; myelin sheath stain. *B*, destruction of myelin sheaths in these tracts; × 50. Marchi stain.

right foot, turned inward on walking. In July 1921 there appeared frequent spasmodic contractions of the left lower extremity, which extended to the muscles of the left upper extremity and back. The gait was dromedary in type. All the dyskinetic movements ceased during sleep and were increased on exertion.

Neurologic Examination.—There were flexion of the left leg and extension of the right leg, with plantar flexion of both feet; occasional extension of the left upper extremity, with pronation and athetosis of the hand, and extreme lordosis and scoliosis (fig. 14 *A*). The involuntary movements were wavelike and were induced by the slightest stimulation. The abductor and flexor muscles and, to a slight extent, the adductor muscles of the right thigh and the muscles of the back were in constant tonic contraction. When the patient was suspended by the upper extremities he presented a picture typical of decerebrate rigidity (fig. 14 *B*): The arms were extended, the fingers partly flexed, the hand and forearm rotated inwardly and the lower extremities hyperextended; the head hung limply forward (fig. 14 *B*). The sternocleidomastoid muscles occasionally showed tonic contracture. The state of the muscles varied between hypotonicity and hypertonicity. When

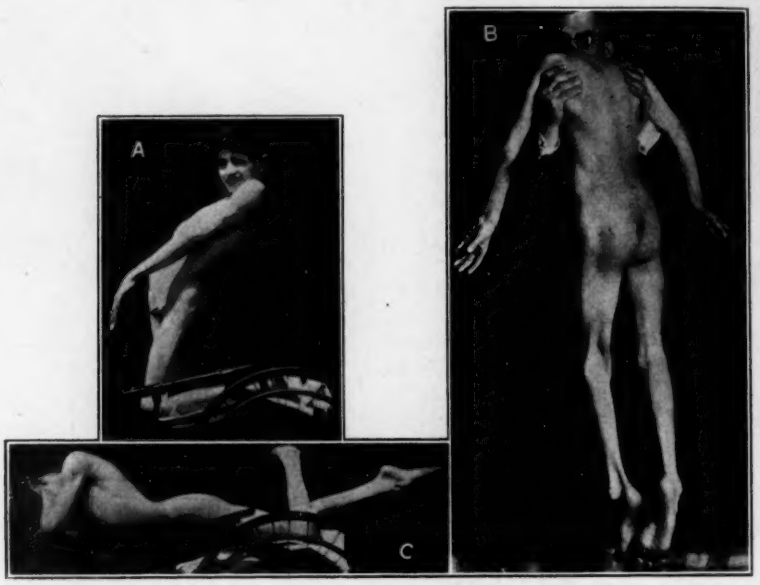

Fig. 14 (case 3).—*A*, dystonic features of the facial muscles, extension of the upper extremities, with pronation and athetosis of the left hand (see *B*), and extreme lordosis and scoliosis. *B*, decerebrate picture, consisting of extension of the arms, inward rotation of the hands and forearms and hyperextension of the lower extremities. The head is not retracted, but hangs limply forward.

the muscles were in a hypertonic state the contractures could be overcome by passive movements. Nystagmus was present on extreme lateral gaze. There were no pathologic reflexes and no sensory disturbances. The cranial nerves were normal.

Course.—The dystonic movements increased in severity and consisted of continuous rotations of the chin to the right, with flexion and rotation of the head to the left. Marked contractures of the lower extremities and tortipelvis developed later. In spite of the dyskinesia and deformities, the patient was able to perform certain skilled movements, such as throwing and bouncing a ball. Administration of large doses of amytal and, finally, of paraldehyde and pentobarbital

sodium, decreased the involuntary movements and produced relaxation. Morphine was tried, but gave no relief. Forced spinal drainage was also attempted, without beneficial results. The patient died suddenly on Jan. 10, 1936.

Laboratory Data.—Studies of the blood, spinal fluid and urine revealed no abnormalities. The blood pressure varied from 120 to 160 systolic and from 80 to 115 diastolic.

Autopsy.—All organs except the central nervous system were normal.

Brain: Grossly, the brain and spinal cord appeared normal. Sections from various parts of the nervous system were stained by the method used in case 1.

Microscopic Examination.—Cerebral Convolutions: Many nerve cells in the second and third cortical layers of the various convolutions were slightly swollen and contained a clear space between the nucleus and the protoplasmic membrane. Some cells showed a collection of Nissl substance at the periphery. There was no increase in the glia nuclei. The changes in these ganglion cells resembled those in edema of the brain, resulting from lead or other intoxications or from pouring water over the brain on its removal.

Basal Ganglia: Examination of the anterior third of the striatum disclosed slight shrinkage and pallor of the putamen and caudate nucleus. In cresyl violet sections the large and a few of the small ganglion cells stained poorly and showed signs of disintegration. The cytoplasmic material of many nerve cells consisted of a few fine granules surrounding the nucleus, with some resemblance to Alzheimer glia cells. Satellitosis was also noted. In places there was a slight increase in the glia nuclei.

In sections through the first segment of the globus pallidus there was poverty of myelin in the caudate nucleus and putamen. The inner segment of the globus pallidus was pale, resembling status dysmyelinisatus, and the dorsolateral pole of the putamen had a slightly marble-like appearance (fig. 15). With a higher power, the fibers of the putamen were seen to stain poorly, but they were not disintegrated; in the area of status marmoratus delicate strands of poorly stained myelin ran in all directions. These dark strands formed anastomoses and encircled small, pale islands of nerve tissue (fig. 15). The pallidal fibers also stained poorly, and a few were swollen and disintegrated; scarcity of myelin fibers was also noted. In cresyl violet preparations some of the nerve cells of the inner segment of the pallidum and of the amygdaloid nucleus were slightly swollen; the nucleus was displaced to the periphery; the tigroid substance was disintegrated, and the remaining cytoplasm was studded with a few pigment granules. The nerve cells of the subthalamic nuclei were normal.

Cerebellum and Dentate Nuclei: There were marked ischemic changes in the nerve cells of the dentate nucleus; the glia cells were increased in size and number.

Brain Stem: In sections of the pons, some of the cells of the nuclei of the fifth, sixth and seventh nerves and of the nucleus of Essick were vacuolated. In sections of the medulla oblongata the nerve cells of the inferior olivary nuclei appeared slightly hypertrophied and vacuolated.

The spinal cord and peripheral nerves were normal.

The consanguinity of the parents in this case was significant.

Case 4.—B. S., a boy aged 10, who was born in the United States, was admitted to the Montefiore Hospital on Aug. 19, 1931. The father was born in the United States, and the mother, in Russia; there was no consanguinity. One

brother is alive and well. There was no mental or nervous disorder in the family. The patient had had the usual diseases of childhood, uncomplicated by nervous manifestations. In August 1928, at the age of 7, there appeared constant, sudden, jerky movements of the right hand, arm and shoulder and, at times, extensor movements of the head; the dyskinesias ceased during sleep. One week later the involuntary movements spread to all the extremities and the head. These symptoms continued until the spring of 1929, when slight improvement was noticed. After a

Fig. 15 (case 3).—Status marmoratus and marked paling of the caudate nucleus and putamen, and status dysmyelinisatus of the inner segment of the globus pallidus. Notice the small, pale islands of nerve tissue in the area of status marmoratus. Myelin sheath stain.

visit to the seashore, an exacerbation of symptoms occurred, and the movements, which became generalized and constant, were occasionally accompanied by peculiar flinging of the hands and jerking of the head.

Neurologic Examination.—The body was bent to the right at the pelvis, making an angle of about 35 degrees with the legs and the head, which was rotated.

During periods of relative rest, lasting from fifteen to thirty minutes, the right upper extremity was held in adduction at the shoulder, in extreme flexion at the elbow and in marked flexion at the wrist and fingers. The left upper extremity was abducted at the shoulder, with an angle of 90 degrees at the elbow, and the fingers were in slight flexion, with a tendency to hyperextension at the metacarpophalangeal joints. The right foot was in slight eversion. Between the intervals of relative rest the following movements were noted: flexion and extension of the left foot and of the fingers of the right hand; pronation and supination of the right forearm; inversion and eversion of both feet, and slight flexion and extension of the right toes. There were marked spasmodic torticollis and coarse tremors of the head. All the movements were aggravated by attention, at times resulting in rapid, wild, flinging, thrashing movements. These assumed the form of an attempt to kick the perineum with the left heel and of wild, rapid, clutching, purposeless movements of the left hand, with the left arm flung over to the head. On effort to squeeze any object with the left hand there resulted facial grimacing, torsion movements of the trunk (tortipelvis), digging of the right fist into the mouth and against the nose, acute flexion at the hips and wild movements of both lower extremities. The muscles were in alternating states of hypotonia and hypertonia. The muscles of the lower extremities were wasted; the sternocleidomastoid muscles were markedly hypertrophied. There were no pathologic reflexes and no sensory disturbances. There were slight weakness of the right side of the face, of the supranuclear type, and some dysarthria. The tongue was also the seat of involuntary movements. The patient's intellect was normal.

Course.—During the last two days of the patient's life nausea and vomiting occurred. He died suddenly on Jan. 7, 1935. He did not receive morphine or sedatives.

Laboratory Data.—Studies of the blood, spinal fluid and urine revealed no abnormalities.

Autopsy.—The stomach was markedly dilated (fig. 16) and filled with black, foul fluid. The mucosa was thin and smooth. Microscopic examination of the stomach showed increased connective tissue in the submucosa, edema of the muscularis, with distention of its fibers, and some parenchymatous changes. The liver was normal.

Brain: The brain weighed 1,400 Gm. and showed no gross abnormalities except slight dilatation of the right lateral ventricle. Sections from various parts of the nervous system were embedded and stained by the methods used in case 1.

Microscopic Examination.—Cerebral Convolutions: Some of the large pyramidal cells of the motor region showed slight disintegration, loss of Nissl substance and pigment atrophy. The microglia cells were slightly increased in number. The other cortical convolutions appeared normal.

Basal Ganglia: There were slight shrinkage and a lacunar appearance of the caudate nucleus and putamen and poverty of nerve fibers in the caudate nucleus. The superior pole of the putamen had a marble-like appearance (fig. 17), as seen in status marmoratus. The area of status marmoratus disclosed dark islands of myelin which formed a network and encircled small, pale islands of nerve tissue. The deeply stained parts contained delicate, poorly stained myelin sheaths, running in all directions. Occasional disintegration of myelin sheaths was noted within the pallidum. The ansa lenticularis was slightly shrunken. In cresyl violet preparations the large ganglion cells of the caudate nucleus and putamen were

decreased in number; some were pale, and others were disintegrated. Hardly a normal large ganglion cell was left; there were marked loss of Nissl substance, displacement of the nuclei to the periphery and satellitosis. Many of the large ganglion cells contained only the nucleus and nucleolus, which were surrounded by a few granules, giving them the appearance of Alzheimer glia cells. The small ganglion cells of the putamen and caudate nucleus also showed slight pathologic changes. In the caudal third of the pallidum there was a slight decrease in the nerve cells; they stained poorly and were surrounded by pigment granules.

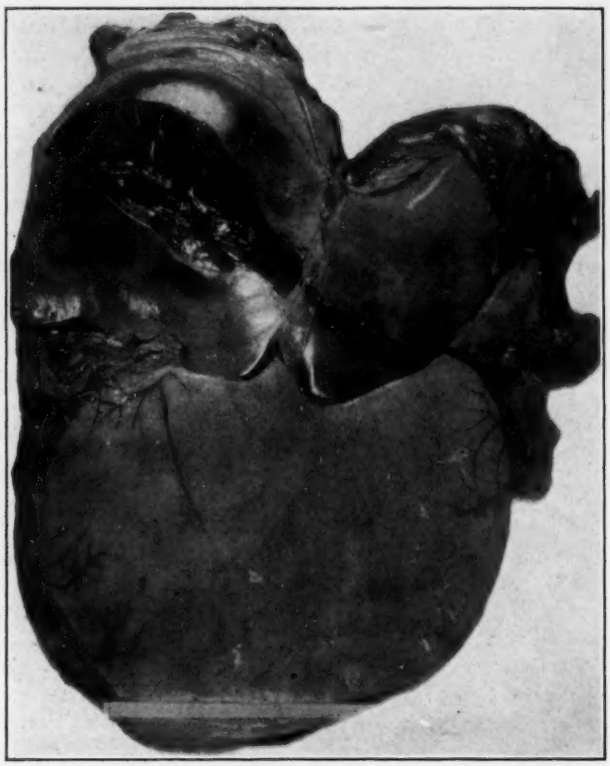

Fig. 16 (case 4).—Extensive dilatation of the stomach.

There was a slight increase in the glia cells in these structures. In sudan III preparations there was a slight accumulation of fat within the pallidal cells and in some of the perivascular spaces. In Holzer preparations slight proliferation of glia fibers was noted in the area of status marmoratus.

The ganglion cells of the corpus Luysi were shrunken and diminished in number; some showed loss of chromatin and peripherally displaced nuclei. There were numerous rod-shaped microglia cells. The nerve cells of the posterior end of the hypothalamus disclosed poverty of pigment granules and slight disintegration.

Cerebellum and Dentate Nuclei: There were marked ischemic changes in the nerve cells of the dentate nuclei and increase in the rod-shaped microglia cells.

Brain Stem: The ganglion cells of the vegetative nuclei of the tenth nerves did not have the usual abundant pigment granules.

Spinal Cord: Sections of the cord were normal.

The progress of the disease in this case was somewhat more rapid than usual. The wild, rapid, clutching, purposeless movements of the

Fig. 17 (case 4).—Status marmoratus of the superior pole of the putamen and darkly stained areas.

left hand, the flinging of the left upper extremity and the wild movements of both lower extremities were thought to be due to the changes in the nerve cells of the corpus Luysi. Of interest were the sudden signs of gastric dilatation before death.

COMMENT

The clinical and pathologic observations in these cases present problems for brief discussion.

Clinical Observations.—All four patients were Jewish, and one or both of their parents were born in Russia or in Russian Poland. A number of observers have claimed that the disorder has a predilection for Jews, especially those born in Russia. Of forty cases of dystonia reported in the literature, the disease was present in only five in which the patients were non-Jews. Of sixteen patients with so-called degenerative idiopathic dystonia whom we observed at the Montefiore Hospital for ten years, the parents of thirteen were Jews, born either in Russia or in Russian Poland. The parents of one patient were born in Rumania, and those of another, in Austria; of the third, one parent only was Jewish. Definite conclusions cannot be drawn from this series, as the majority of the patients in this institution are of Jewish origin. The parents of the third patient, on whom necropsy was performed, were cousins. The disorder was not found in other members of the families of the patients on whom autopsy was performed. A familial incidence was found in the following instances in our clinical series: two sisters and one brother and, recently, a fourth member of the same family of one patient; a sister, brother and paternal aunt of another patient, and the mother of still another, who showed dyskinesia in the form of a fragment of dystonia. The disease was reported to be present in siblings by Schwalbe,[1] Bernstein,[6] Jakob,[7] Mankowsky and Czerny[8] and Kehrer.[9] Price[10] described the disorder in twins, and Wechsler and Brock,[11] Davidenkow and Zolotowa[12] and others mentioned a familial incidence.

A survey of the literature showed an incidence of 60 per cent in males and 40 per cent in females; however, of the twenty patients with

6. Bernstein, S.: Ein Fall von Torsionskrampf, Wien. klin. Wchnschr. **25**: 1567, 1912.

7. Jakob, A.: Zur Frage der nosologischen und lokalisatorischen Auffassung der torsiondystonischen Krankheitserscheinungen, Deutsche Ztschr. f. Nervenh. **124**:148, 1932.

8. Mankowsky, B. N., and Czerny, L. J.: Zur Frage der Heredität der Torsiondystonie, Monatschr. f. Psychiat. u. Neurol. **72**:165, 1929.

9. Kehrer, F.: Die erblichen Nervenkrankheiten, Deutsche Ztschr. f. Nervenh. **83**:201, 1924.

10. Price, G. E.: The Simultaneous Occurrence of Dystonia Lenticularis in Twins, Arch. Neurol. & Psychiat. **5**:768 (June) 1921.

11. Wechsler, I. S., and Brock, S.: Dystonia Musculorum Deformans, with Especial Reference to a Myostatic Form and the Occurrence of Decerebrate Rigidity Phenomena, Arch. Neurol. & Psychiat. **8**:538 (Nov.) 1922.

12. Davidenkow, S. N., and Zolotowa, N. A.: Eine Familie mit Torsionspasmus, Mitt. a. d. Staatl. Univ., Baku **1**:151, 1921.

degenerative dystonias in our series, nine were males and eleven females. Of six patients with postencephalitic dystonia observed by us clinically, two were males and four females. The disease in the idiopathic group begins in most instances in childhood or at about puberty. The occurrence of the disorder at the age of 6 years in case 1 was unusually early. Navarro and Marotta [13] mentioned the appearance of the disease in a patient 4 years of age. The age distribution of our patients was as follows: Of those with degenerative dystonia, there were eight in the first and twelve in the second decade; of those with encephalitic dystonias, there were one each in the first and second decades, and two each in the third and fourth decades.

In a few instances of dystonia a familial history of alcoholism, epilepsy, migraine, tics, chorea and psychosis was reported. In a previous case described by us,[14] typical migrainous attacks developed three years before death. In a number of cases the dystonia immediately followed an infectious disease, such as encephalitis lethargica, exanthematous diseases or chorea. In case 1 in our series paralysis of the right arm developed after an attack of coughing during pertussis. The patient recovered completely; as the dystonia did not appear until six years later, we believe that there was no direct relationship between the whooping cough and the dyskinesia. A case of dystonia following whooping cough was described by Climenko.[15] Trauma was considered as a precipitating factor in some instances. The dyskinesia in case 2 appeared immediately after a fright caused by a thunder storm. A traumatic history was obtained in three of the twenty-six cases observed by us.

Clinically, our cases conformed to those described in the literature. A few of the unusual neurologic findings in the present series merit consideration. In cases 1 and 2 there was facial grimacing, and in cases 1 and 3 athetoid movements of the fingers appeared. These signs, uncommon in dystonia, have been reported. Slight facial paresis, observed in cases 2 and 4, was also described by Davidenkow and Zolotowa [12] and others. Dysarthria, as noted in cases 1 and 4, is rare. Disturbances of speech, reported by Keschner [16] and others, which are most frequent in postencephalitic dystonia, indicate that the muscles of articulation, like other muscles, may become involved. Bilateral winking movements, noted in case 2, were also reported by others. Nystagmus, present in case 3, was described by Wechsler and Brock [11]

13. Navarro, J. C., and Marotta, A. S.: Dystonia musculorum deformans ou spasme de torsion, Arch. de méd. d. enf. **30**:29, 1927.

14. Davison, C., and Goodhart, S. P.: Dystonia Musculorum Deformans: A Clinicopathologic Study, Arch. Neurol. & Psychiat. **29**:1108 (May) 1933.

15. Climenko, H.: Dystonia Musculorum Deformans, M. Rec. **86**:1000, 1914.

16. Keschner, M.: Dystonia Musculorum Deformans, J. Nerv. & Ment. Dis. **47**:107, 1918.

in three instances. Of interest in our cases were the partial picture of decerebrate rigidity observed in cases 2 and 3 and the massive flinging movements in cases 1 and 4; the corpus Luysi in cases in which there were ballistic movements showed pathologic changes. Wasting of the muscles without fibrillations, as reported by others, was noted in cases 2 and 4. These atrophies, due to disuse and not to disease of the anterior horn cells, were present in muscles of the extremities which showed permanent contractures.

There were disturbances of the vegetative nervous system throughout the course of the disease in case 2, and shortly before death in case 4. In case 2 these consisted of obstipation, abdominal distention and pain, protracted nausea and incessant vomiting, retention of urine and spasm of the urethra, tachycardia and paroxysms of dyspnea. Similar observations were noted by Kaufman, Savitsky, and Freid [17] in cases of encephalitic dystonia. Our patients did not have encephalitis, and histopathologically the neural changes were not those characteristic of this disease. Degenerative changes were observed in the nerve cells of the hypothalamic nuclei. These lesions indicate that the visceral musculature, possibly controlled by the hypothalamus or the striatum, may be subjected to the same dyskinetic phenomena as the somatic musculature.

The dystonic movements in all our cases disappeared during sleep and were aggravated by attention or emotion. In case 4, as in many instances of extrapyramidal disease, the patient, in spite of the marked dyskinesia, was able to perform highly skilled acquired acts.

Pathologic Changes and Pathogenesis.—The pathologic process in the four cases in this series was most pronounced in the striatum (putamen and caudate nucleus) and the dentate nucleus. There were slight shrinkage and status marmoratus in three cases, marked status fibrosus and shrinkage of the putamen in one and status dysmyelinisatus in another. In case 1 the claustrum and inferior olivary nuclei were also involved. Diminution in number and marked destructive changes were observed in the large nerve cells of the striatum in all cases. The changes in the small nerve cells of the striatum were less extensive. The nerve cells of the globus pallidus, especially those of the inner segments, were slightly diseased in all cases. Some of the nerve cells in the corpus Luysi in cases 1 and 4 revealed pathologic changes. The nerve cells of the dentate nucleus showed marked ischemic cell changes, similar to those in vascular spasm, in three instances; in case 2 the nerve cells showed chromatolysis and chronic cell changes. In none of the cases was there evidence of an inflammatory or atherosclerotic process.

17. Kaufman, M. R.; Savitsky, N., and Freid, J. R.: Dystonia Musculorum Deformans of Encephalitic Etiology, Arch. Neurol. & Psychiat. **20**:824 (Oct.) 1928.

In case 3 the nerve cells of the various cortical convolutions, the nuclei of the fifth, sixth and seventh nerve, the nucleus of Essick and the olivary nuclei showed changes similar to those resulting from drug or paraldehyde intoxication; these, surely, were not responsible for the dyskinesia in these cases. In a previous case of dystonia,[14] we reported vacuolation in the nerve cells of the nuclei of the sixth, seventh, ninth, tenth, eleventh and twelfth cranial nerves and in the anterior horn cells. We believed then that these lesions were chance associations, the cause of which we were unable to explain. In this instance, however, the changes may have been due to paraldehyde intoxication.

In case 1 there were distortion in the arrangement of the cyto-architectural layers and marked disease of the nerve cells in the frontal, premotor, motor, insular, superior parietal, angular and supramarginal gyri. In case 4 the large pyramidal cells in the premotor and motor regions showed slight pathologic changes. Changes in the nerve cells in the postcentral superior parietal and insular convolutions were reported by us[14] and others. Van Bogaert[18] observed a tuberculoma of the parietal lobe in a case of dystonia in which the striatum was not involved. Munch-Petersen[19] reported dystonia in a case of a diffuse inflammatory process in the cerebral cortex, especially the frontal lobes, in which there were no abnormalities in the basal ganglia. Extrapyramidal functions were ascribed (Foerster,[20] Fulton and his associates[21] and Tower[22]) to some of the cortical convolutions. Poljak,[23] on the basis of lesions of the premotor area, traced extrapyramidal fibers which passed from this area through the internal capsule into the cerebral peduncles, with perhaps connection with the caudate nucleus, and disappeared into the gray matter of the substantia nigra and the pontile nuclei. Whether the involvement of convolutions in our cases was partly responsible for the dyskinetic phenomena is problematic. Excision of the premotor area in case 1 did not result in amelioration of the dyskinesia.

In the two cases in which there were vegetative disturbances the nerve cells of the hypothalamic nuclei did not contain the usual amount of pigment. We are hesitant to ascribe the vegetative symptoms to

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18. van Bogaert, L.: Observations anatomiques et cliniques de spasmes de torsion, Rev. neurol. **1**:923, 1929.

19. Munch-Petersen, C. J.: Beiträge zur Frage des pathologisch-anatomischen Substrats der Torsionsdystonie, Acta psychiat. et neurol. **10**:391, 1935.

20. Foerster, O.: The Motor Cortex in Man in the Light of Hughlings Jackson's Doctrines, Brain **59**:135, 1936.

21. Fulton, J. F.; Liddell, E. G. T., and Rioch, D. M. K.: Relation of the Cerebrum to the Cerebellum, Arch. Neurol. & Psychiat. **28**:542 (Sept.) 1932.

22. Tower, S. S.: Extrapyramidal Action from the Cat's Cerebral Cortex: Motor and Inhibitory, Brain **59**:408, 1936.

23. Poljak, cited by Darrow, C. W.: Neural Mechanisms Controlling the Palmar Galvanic Skin Reflex and Palmar Sweating, Arch. Neurol. & Psychiat. **37**: 641 (March) 1937.

these minor pathologic changes, as we have seen such lesions associated with other conditions without associated vegetative disturbances. The possibility of striohypothalamic connections may account for the vegetative symptoms.

Status marmoratus, which was noted in the striatum in three instances (cases 1, 2 and 3), has been described by the Vogts [24] as a developmental anomaly in cases of *athétose doublée* and other extrapyramidal disorders. In contrast to our observations and those reported by C. and O. Vogt, état marblé was observed not only in the striatum but in the cortex and other neural structures by Bielschowsky [25] and others. Meyer,[26] Scholz,[27] Löwenberg and Malamud [28] and others have shown that this marble-like appearance may occur also in inflammatory or vascular disease. The myelination of the gliotic areas is explained on the basis of actual regeneration of axis-cylinders, myelination of preexisting axis-cylinders or a purely mechanical condensation of preexisting myelinated nerve fibers. In our cases we saw no evidence of actual regeneration of axis-cylinders.

Status dysmyelinisatus, consisting in a poverty of myelin fibers in the putamen in case 1 and in the inner segments of the pallidum in cases 1, 2 and 3, has been described by C. and O. Vogt,[24] Hallevorden and Spatz,[29] Winkelman [30] and others in states of progressive rigidity. A similar process was described by one of us (C. D.) [31] in two adults suffering from spastic pseudosclerosis. Status dysmyelinisatus associated with dystonia was also reported by Guillain, Mollaret and Bertrand [32]

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24. Vogt, C., and Vogt, O: Zur Lehre der Erkrankungen des striären Systems, Leipzig, J. A. Barth, 1920.

25. Bielschowsky, M.: Ueber den Status marmoratus des Striatum und atypische Markfasergeflichte der Hirnrinde, J. f. Psychol. u. Neurol. **31**:125, 1924.

26. Meyer, A.: Zur Auffassung des Status marmoratus, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:529, 1926.

27. Scholz, W.: Zur Kenntnis des Status marmoratus, Ztschr. f. d. ges. Neurol. u. Psychiat. **88**:355, 1924.

28. Löwenberg, K., and Malamud, W.: Status Marmoratus, Arch. Neurol. & Psychiat. **29**:104 (Jan.) 1933.

29. Hallevorden, J., and Spatz, H.: Eigenartige Erkrankung im extrapyramidal-motorischen System. Ein Beitrag zu den Beziehungen zwischen Globus pallidus und Substantia nigra, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:254, 1922.

30. Winkelman, N. W.: Progressive Pallidal Degeneration, Arch. Neurol. & Psychiat. **27**:1 (Jan.) 1932.

31. Davison, C.: Spastic Pseudosclerosis (Cortico-Pallido-Spinal Degeneration), Brain **55**:247, 1932.

32. Guillain, G.; Mollaret, P., and Bertrand, I.: Etude clinique, cinématographique et anatomo-pathologique d'un grand spasme de torsion postencéphalitique, Rev. neurol. **41**:342, 1934.

and by Laruelle and van Bogaert.[33] The alternating hypertonic state of the muscles in some of our cases may have been due partly to disease in the pallidum.

Status fibrosus, or *état fibreux,* noted in the striatum in case 1, consisted of a twofold process: intense gliosis and hypermyelinated areas, which were best seen in the putamen. The gliosis undoubtedly is a replacement of destroyed neural tissue, whereas the hypermyelinated areas probably represent mechanical condensation of the existing myelin fibers due to shrinkage of the tissue or regeneration of myelinated axis-cylinders.

The involvement of the dentate nuclei is of importance, as these nuclear masses have been implicated in a number of other instances (Urechia, Mihalescu and Eleckes;[34] Jacob,[7] in cases 1 and 2, Schmitt and Scholz;[35] Agostini,[36] and Poppi.[37] The uniform ischemic changes in the nerve cells of the dentate nuclei are possibly the end-result of transient vascular spasms with resulting anemia, as described by Spielmeyer[38] in cases of epilepsy. The changes in the dentate nucleus appeared to be of recent origin, except in case 2. For this reason we believe that one may be dealing with a biochemical disturbance, the products of which attacked the blood vessels (vasospasm) or the nerve cells of these two vulnerable structures—the striatum and the dentate nucleus. The ischemic cell changes in the dentate nuclei support the theory of vasospasm.

The changes in the dentate nuclei observed in our cases raise the question of the role these nuclear masses play in extrapyramidal disorders. Spatz[39] and others expressed the belief that these structures are part of the extrapyramidal system, related histologically and physiochemically to the pallidum. Guillain, Mathieu and Bertrand,[40] Horsley

33. Laruelle, L., and van Bogaert, L.: Etude anatomo-clinique d'un cas de syndrome rigide avec spasme de torsion, Rev. neurol. **1**:941, 1929.

34. Urechia, C. I.; Mihalescu, S., and Eleckes, N.: Contribution anatomo-clinique a l'étude de la dystonie lenticulaire (spasme de torsion), Rev. neurol. **32**:177, 1925.

35. Schmitt, W., and Scholz, W.: Klinischer und pathologisch-anatomischer Beitrag zur Torsiondystonie, Deutsche Ztschr. f. Nervenh. **126**:53, 1932.

36. Agostini, C.: Sopra un caso di spasmo di torsione in encefalitis epidemica cronica, Riv. di pat. nerv. **43**:440, 1934.

37. Poppi, V.: Beitrag zur pathologischen Anatomie der Torsiondystonie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **61**:503, 1931.

38. Spielmeyer, W.: Die Pathogenese des epileptischen Krämpfes, Ztschr. f. d. ges. Neurol. u. Psychiat. **109**:501, 1927.

39. Spatz, H.: Ueber den Eisennachweis im Gehirn besonders im Zentren des extra-pyramidal-motorischen Systems, Ztschr. f. d. ges. Neurol. u. Psychiat. **77**: 261, 1922.

40. Guillain, G.; Mathieu, P., and Bertrand, I.: Etude anatomo-clinique sur deux cas d'atrophie olivo-ponto-cérébelleuse avec rigidité, Ann. de méd. **20**:417, 1926.

and Clarke [41] and Foerster [42] described hypertonic states associated with diseases of these nuclear complexes.

The involvement of the inferior olivary nuclei in case 1 is significant. Generalized hypertonia due to vascular lesion of the inferior olivary nuclei was described by Guillain, Bertrand and Mathieu.[43] Furthermore, Besta [44] succeeded in producing catatonia in cats by sectioning the olivocerebellar fibers. Luthy [45] expressed the belief that the symptoms following disease of the olives are not different from those produced by rubrospinal lesions.

The question of somatotopic localization within the striatum in cases of dystonia is of importance. The dyskinesia and the pathologic changes in the striatum in our cases were too diffuse to permit us to say definitely whether segmental localization, as postulated by Mingazini [46] and C. and O. Vogt,[24] exists in the striatum. Even in the cases reported by Cassirer and Bielschowsky [47] and by Alpers and Drayer,[48] in which the dystonia was confined to the muscles of the neck, the changes observed in the striatum were not limited to a specific area. On the basis of clinical experience, we believe in the possibility of somatotopic localization in the striatum, but we are not able to specify the nature of this segmental cyto-architectural arrangement.

The liver in our cases was not involved. Thomalla,[49] Wimmer [50] and Jakob [7] (case 3) described cirrhosis of the liver. Because of the associated pathologic condition of the liver in the cases reported by these authors, Wimmer and others expressed the belief that dystonia mus-

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41. Horsley, V., and Clarke, R. H.: The Structure and the Functions of the Cerebellum Examined by a New Method, Brain **31**:45, 1908.

42. Foerster, O.: Die arteriosklerotische Muskelstarre, Allg. Ztschr. f. Psychiat. **66**:902, 1909.

43. Guillain, G.; Bertrand, I., and Mathieu, P.: La rigidité d'origine olivaire, Ann. de méd. **25**:460, 1929.

44. Besta, C.: Sulla funzione delle olive bulbari, Boll. d. Soc. ital. di biol. sper. **7**:8, 1932.

45. Luthy, F.: Les relations anatomiques de l'olive inférieure avec le cervelet, Rev. neurol. **2**:516, 1931.

46. Mingazini, G.: Das Linsenkernsyndrom, Ztschr. f. d. ges. Neurol. u. Psychiat. **8**:85, 1912.

47. Cassirer, R., and Bielschowsky, M.: Halsmuskelkrampf und Torsionspasmus, Klin. Wchnschr. **1**:53, 1922; Zentralbl. f. d. ges. Neurol. u. Psychiat. **28**:513, 1922.

48. Alpers, B. J., and Drayer, C. S.: The Organic Background of Some Cases of Spasmodic Torticollis: Report of Case with Autopsy, Am. J. M. Sc. **193**:378, 1937.

49. Thomalla, C.: Ein Fall von Torsionspasmus mit Sectionsbefund, Ztschr. f. d. ges. Neurol. u. Psychiat. **41**:311, 1918.

50. Wimmer, A.: Etudes sur les syndromes extra-pyramidaux: Spasme de torsion progressive infantile, Rev. neurol. **37**:952, 1921.

culorum deformans is merely a clinical variant of extrapyramidal disorders, such as hepatolenticular degeneration. It should be emphasized that severe psychic disorders are usually not present and that pigmentation at the corneoscleral junction (Kayser-Fleischer ring), as seen in many instances of hepatolenticular degeneration, has never been described in cases of dystonia. Fränkel [51] and Tschetwerikoff [52] found high grade imbecility in their cases of dystonia. Schwalbe [1] described delirium in one instance, and Kleist and Herz [53] reported so-called progressive paranoia in another. In a careful review of our twenty-six cases of dystonia, we did not find psychotic manifestations. Familial incidence in cases of hepatolenticular degeneration is frequent, and dysphagia and dysarthria are also more common. Although some of the extrapyramidal disorders, especially postencephalitic conditions, may pass from hyperkinesia and hypotonicity to hypokinesia and hypertonicity, we still believe that each disease represents a specific clinical entity. Dystonia may be related to Wilson's disease, but the frequent alterations in tonus and the usual absence of rigidity and cirrhosis of the liver make it a separate clinical syndrome. The cases in which there was cirrhosis of the liver were probably instances of hepatolenticular degeneration. The main lesion in both diseases is in the striatum, but histopathologically the two differ in that in dystonia there is absence both of cirrhosis of the liver and of typical Alzheimer glia cells.

SUMMARY AND CONCLUSIONS

Four cases of dystonia musculorum deformans are described clinicopathologically.

Clinically, in all four cases there were typical dystonic manifestations. The clinical symptoms early in the course of the disease in case 2 were similar to those seen in hysteria. Later, however, definite dystonic movements appeared. In case 1 and 4 some of the dyskinetic phenomena resembled hemiballismus. Disturbances in the vegetative nervous system were noted throughout the disease in case 2 and shortly before death in case 4.

Histopathologically, the main lesions in these instances were in the striatum (putamen and caudate nucleus) and the dentate nucleus. Status marmoratus and status dysmyelinisatus were observed in three cases,

51. Fränkel, F.: Demonstration zum dystonischen Syndrome, Zentralbl. f. d. ges. Neurol. u. Psychiat. **36**:254, 1924.

52. Tschetwerikoff, N.: Zur Kasuistick des Torsionspasmus, Russk. klin. **1**:350, 1924.

53. Kleist and Herz, cited by Mendell, K.: Torsiondystonie, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 16, pp. 848-870.

and status fibrosus, in one. The outstanding changes in the ganglion cells in these structures, except in case 2, consisted of ischemic changes. In cases 1 and 4, in which there were massive flinging movements, disease of the corpus Luysi was also disclosed. In cases 2 and 4, in which there were disturbances of the vegetative nervous system, the nerve cells of the hypothalamic nuclei did not contain the usual amount of pigment granules. The claustrum and inferior olivary nuclei in case 1 were also involved. The nerve cells of the globus pallidus, especially those of the inner segments, were slightly diseased in all cases. In case 1 there was also extensive disease of the nerve cells in the frontal, premotor, motor, insular, superior parietal, angular and supramarginal gyri.

The role of the striatum and dentate nuclei in the causation of extrapyramidal disorders and the relation of dystonia to these dyskinesias are discussed. Dystonia musculorum deformans, although a variant of extrapyramidal disorders, is a specific clinical entity and can be differentiated from hepatolenticular degeneration and chorea.

DISCUSSION

Dr. Samuel Brock, New York: A study of four cases of dystonia musculorum deformans from the neuropathologic point of view is a unique contribution. Ideas about this disease are changing. The syndromic grouping is not as pure as it was once thought, although there is a fundamentally characteristic motor disturbance.

Etiologically, it does not seem to be a specific disease. Moreover, it will be noted that certain clinical appendages are added to this motor disturbance, viz., visceromotor effects and signs of involvement of the cranial nerves, especially nystagmus. Then, again, it becomes apparent that the motor disturbances are not all of one sort—choreiform, hemiballistic, athetoid and wing-beating movements, together with myoclonic twitches, are found, and yet the basis of all this is the characteristic torsion movement in which hypertonus and hypotonus flow into one another.

In 1922 Wechsler and I pointed out that the kinetic disorder is fairly common and well known but that there is an infrequent form of the disease, a frozen postural fixation, which we called the myostatic type. The problem that faces the neuropathologist is correlation of the clinical signs with the neuropathologic changes; here one is still in the realm of doubt. How are the movements or the postural fixation brought about? Is a certain complicated arc released, or are the activities of unusual nerve circuits (formerly closed) brought into an open orbit, as was suggested by Kubie?

There is a question concerning neuropathologic changes which I should like to ask Dr. Davison: What is the significance of the ischemic nerve cell changes? Is he able to cast any light on the multiple etiologic factors which it is believed produce this disorder?

Dr. Israel S. Wechsler, New York: Dr. Brock has touched on a number of points which have interested us for many years. I wish to discuss the problem of movement. If the pathologic description holds true in other cases—it will be recalled that previous examinations showed lesions scattered throughout the

brain, from the cortex to the medulla, pons and cerebellum—it seems that the dentate and caudate nuclei bear the brunt of the process in dystonia.

From the clinical description of the cases, it is quite evident that one is dealing with one clinical entity. The first case does not belong to the group of dystonias of the Ziehen-Oppenheim type. The child became ill at the age of 6 months, with evidences that the process involved various parts of the nervous system.

It seems advisable to consider dystonia not as a disease but as a symptom. If this is done, there is the possibility of adding to understanding of the pathophysiology of movement. Chorea, too, is a symptom and not a disease. It is true that in certain instances the clinical picture is dominated by a single symptom, and so there are chorea minor and Huntington's chorea; but there are other cases in which chorea is but one symptom among many. The same is true of dystonia.

Movements of chorea are similar to those of dystonia. Chorea is a rapid, less ample form of dystonia, and dystonia is an amplified, slow movement of chorea. The distribution differs, but there is a certain pattern in the movement of both diseases. One may say that both chorea and dystonia are subjectively purposeful and objectively purposeless movements. The patient tries to do something and to get somewhere, but never succeeds.

It is of interest that involvement of the same part of the nervous system can give rise to chorea and to dystonia. Injury of the caudate nucleus may result in chorea. In two of the cases of dystonia the caudate nuclei were involved. Involvement of the corpus Luysi results in hemiballismus, which may be conceived of as rapid dystonia of an ample sort. The dentate nucleus, so far as chorea is concerned, is also important in that cases of what the Germans call the *Bindearm* (brachium conjunctivum) type of chorea have been described.

Here, then, is a symptom which is characterized both by movement and by posture. It is necessary to remember that the extrapyramidal system—and I agree with those who think that the word "extrapyramidal" is too loosely used—is not one structure. There are at least three or four systems. In the present state of knowledge, it is impossible to say which is responsible for the movements. It may be that dystonia is due to disease of the striatum and that disturbance in posture is a motor expression of pallidal disease. We know that in paralysis agitans the essential disturbance is one of posture and tonus. There is no true paralysis, and there need not be tremor. In dystonia we have precisely the two characteristics, namely, a postural disturbance which colors the movement and a constant variability in tonus.

The contribution of Drs. Goodhart and Davison may be of value in throwing light on the anatomic localization. Unfortunately, this disease does not lend itself to exact physiologic, anatomic and clinical correlation. However, I should like to emphasize once more the need for considering dystonia not as a disease but as a symptom which can occur on the basis of any number of pathologic processes, and possibly as the result of lesions in various parts of the nervous system.

Dr. Charles A. McKendree, New York: May I ask Dr. Davison if any special studies were made of the red nucleus, especially in the case in which there were mild hemiballistic movements?

Dr. Smith Ely Jelliffe: I wish simply to contribute a short historical note and to add my approval of Dr. Wechsler's point of view regarding the purely symptomatic or syndromic aspect of a *cohors moborum*, which has been called "dystonia musculorum deformans."

It was my pleasure in 1909 and 1910 to spend six months in the clinic of Professor Ziehen, in Berlin, and for six months I saw every day the three classic

siblings, on the basis of whose cases was erected the Schultz monograph, in which the original description of the syndrome was given. It was evident from the kaleidoscopic appearances of these three children that all that has been emphasized by Dr. Wechsler is true.

Dr. S. Philip Goodhart, New York: Case 2 was originally one of a group of cases of dyskinesias presented before a meeting of the association in 1921 by Dr. Tilney and me in our study of deformities of motion by means of what we termed bradykinetic analysis. The condition was for several years regarded as psychogenic. The especial interest in the case lies in the fact that the disease appeared to represent a transition from a so-called functional to a definite organic syndrome.

Dr. Charles Davison: Dr. Brock has asked a pertinent question, namely, the significance of the ischemic cell changes in these degenerative diseases. All are familiar with the so-called ischemic cell changes in the cornu ammonis in cases of epilepsy, as described by Spielmeyer and his co-workers. I wonder whether one is not dealing with a similar phenomenon in the dystonias. The vessels in the cases reported, except for the proliferation in the areas involved in the first case, did not show pathologic changes. Whether one is confronted in dystonia with certain metabolic, biochemical disturbances, which, in turn, induce vasospasm of the vessels with some form of anemia and lead finally to the ischemic cell changes, is an open question. Dr. Brock's second question, whether I can cast light on the multiple etiologic factors operating in this disorder, is also difficult to answer. All are familiar with the number of cases of so-called dystonia which appeared after the epidemic of encephalitis lethargica. None of the four patients in this series had a history or histopathologic evidence of an encephalitic process. Observers were certain that the dystonia in these cases was not the result of infection. The patients were Jewish, and a history of consanguinity was found only in one instance. Because of these facts and the absence of evidence of infection, we were inclined to consider the disease as idiopathic dystonia, of unknown etiology. I do not know whether the term degenerative is appropriate, but in the absence of a better name the disturbance can be designated as degenerative or idiopathic dystonia.

Cases of dystonia are reported in which other factors were operative. Cases of dystonia due to infection, or even tumor or vascular disease, have also been described.

With reference to the comments by Dr. Wechsler and Dr. Jelliffe: I must agree with Dr. Wechsler that dystonia is not a clearcut disease; however, I object to the use of the word "symptom"; rather, I should substitute Dr. Jelliffe's suggestion of a "syndrome or symptom complex" of extrapyramidal disease. I say a "syndrome" of extrapyramidal disease because, clinically, one is able to differentiate dystonia, chorea and hepatolenticular degeneration. In spite of occasional difficulties, the condition can be diagnosed clinically in most cases.

It is true that in two of the cases we described there were suggestive hemiballistic movements. The corpus Luysi in these cases showed minor lesions. These movements should not rule out the diagnosis of dystonia.

In answer to Dr. McKendree's question, I wish to state that the red nucleus was intact not only in the cases in which there were hemiballistic movements but in all cases. The red nucleus has been considered by some to be responsible for extrapyramidal disorders. In my experience with pathologic changes in diseases of the extrapyramidal system, I found the red nucleus better preserved than any other structure of the extrapyramidal system.

ACID-BASE BALANCE OF THE BLOOD IN A PATIENT WITH HYSTERICAL HYPERVENTILATION

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Changes in structure or function that are associated with psychogenic manifestations are worthy of attention and intensive investigation. In this communication are reported the significant changes in the physicochemical equilibrium of the blood in a patient with hysterical hyperventilation. The principal shift in the acid-base balance of the blood was toward alkalosis; the discussion of the biochemical changes, therefore, will begin with a résumé of this condition. In order that this presentation may approach completeness in detail, an extended psychiatric history is included.

In clinical investigation two varieties of alkalosis are differentiated chemically and may be studied independently—metabolic and respiratory alkalosis. Metabolic alkalosis, or excess of alkali, follows the ingestion of large amounts of alkali or the loss of fixed acid. Patients with this condition show an increase in the partial pressure of carbon dioxide in arterial blood (pCO_2), an increase in the concentration of bicarbonate $(HCO_3)_s$ in the serum and a decrease in hydrogen ion concentration.[1] Respiratory alkalosis, or carbon dioxide (CO_2) deficit, is associated with hyperventilation of varying durations. Accompanying induced or spontaneous hyperventilation, the p_{H_s} is increased as in metabolic alkalosis, and the contrasting changes are decreased pCO_2 and decreased $(HCO_3)_s$. These changes are transient in experimental hyperventilation of short duration, and the movement of fixed acid and fixed base in the body is

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1. p_H, the symbol for hydrogen ion concentration, varies inversely as the true concentration (H^+).

small. There are few observations reported on respiratory alkalosis of long duration, and most ideas concerning permanent shift of fixed acid and fixed acid base have been dervied from speculation.[2]

In the literature there are reports on three patients with hyperventilation of long duration. In 1922 Essen, Kauders and Porges [4] observed an arterial pCO_2 of about 18 mm. of mercury in a patient with persistent hyperventilation following encephalitis. The changes in the carbon diox-

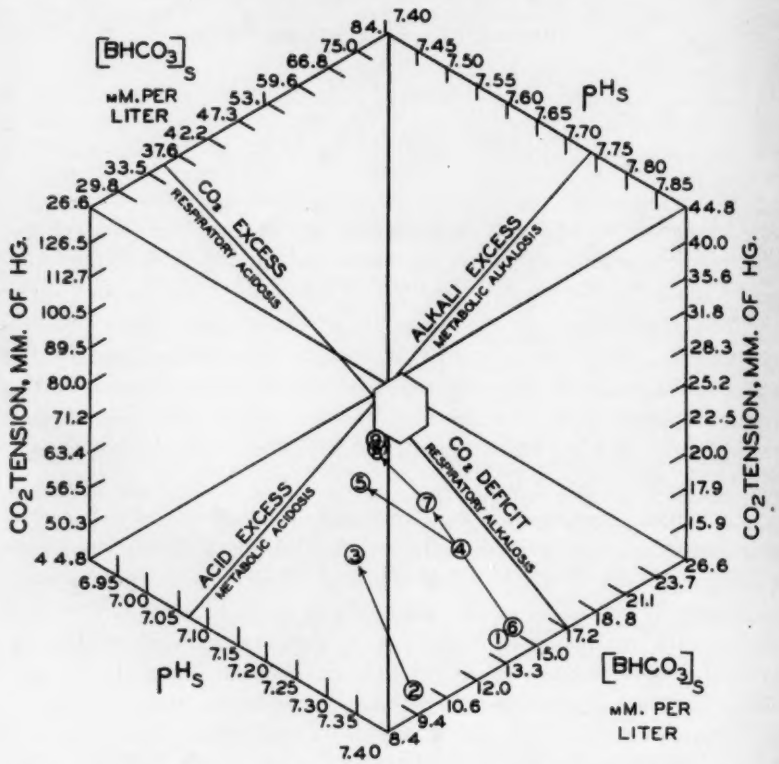

Chart for the acid-base balance showing position of the several samples. The arrows are drawn between two or more specimens of blood taken during a single day's experiment.

ide content of the blood were not reported, but after a night's rest, with cessation of hyperventilation, the serum chloride concentration decreased

2. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, p. 956.

3. Footnote deleted on proof.

4. Essen, H.; Kauders, F., and Porges, O.: Die Beziehungen der CO_2-Spannung der Alveolarluft zu den Chloriden des Blutserums, Wien. Arch. f. inn. Med. **5**:499, 1922.

2.4 milliequivalents (m. eq.) per liter. One year later, Harrop and Loeb [5] reported observations on the blood obtained one hour before death from a patient who had had hyperventilation for three days. At the time the blood was drawn the respiratory rate varied from 40 to 50 per minute. The p_H of the arterial serum was 7.59. The third patient with prolonged hyperventilation was studied by Peters, Bulger, Eisenman and Lee,[6] who found an increased concentration of chloride and fixed base in the serum. The p_{H_s} was below 7.4. From the data obtained on these three patients, all of whom had encephalitis, Peters and Van Slyke [6a] came to the conclusion that the ultimate compensation for plasma bicarbonate is accomplished by a reciprocal shift of chloride. There are no studies of the blood following prolonged psychogenic hyperventilation.

In this communication there are presented the changes in the blood of a woman 21 years of age who suffered from respiratory alkalosis of long duration. She was admitted to the psychiatric service of the Massachusetts General Hospital with a diagnosis of hysterical hyperventilation and tetany. Her chief complaint was rapid breathing for approximately six weeks. The respiratory rate was more than 100 per minute on many occasions after admission. The patient was studied in the hospital for four months, and no significant abnormality was found except tetany, alkalosis, choreic movements and hysterical mentality. The hyperventilation and tetany subsided after the prolonged efforts of several physicians and the members of a religious order. At the time of discharge the respiratory rate had been below 20 per minute for nearly four weeks.

METHODS

The analytic methods used in this study have been described previously.[7] Blood from the brachial artery was taken on nine occasions, over a period of nineteen days. The patient had been fasting for at least eight hours before each sample was taken. No significant change in the respiratory rate was observed during any of the arterial punctures. The partial pressure of carbon dioxide in the arterial blood was determined indirectly by the method of Bock and Field.[8] One point for the construction of the carbon dioxide dissociation curve was obtained by analysis of the blood and gas equilibrated in a tonometer at 37.5 C. The value for the con-

5. Harrop, G. A., and Loeb, R. F.: Uncompensated Alkalosis in Encephalitis, J. A. M. A. **81**:452 (Aug. 11) 1923.

6. Peters, J. P.; Bulger, H. A.; Eisenman, A. J., and Lee, C.: Total Acid-Base Equilibrium of Plasma in Health and Disease: IV. The Effects of Stasis, Exercise, Hyperpnea, and Anoxemia, and the Causes of Tetany, J. Biol. Chem. **67**:176, 1926.

6a. Peters and Van Slyke,[2] p. 957.

7. Talbott, J. H., and Michelsen, J.: Heat Cramps: A Clinical and Chemical Study, J. Clin. Investigation **12**:533, 1933. Talbott, J. H.; Jacobson, B. M., and Oberg, S. A.: The Electrolyte Balance in Acute Gout, ibid. **14**:411, 1935.

8. Bock, A. V., and Field, H., Jr.: The Carbon Dioxide Equilibrium in Alveolar Air and Arterial Blood, J. Biol. Chem. **62**:269, 1924.

centration of carbon dioxide in arterial blood was applied to the derived carbon dioxide dissociation curve. This method has been shown to be satisfactory for the determination of arterial pCO_2.[9]

Values for p_H were derived from the equation

$$p_{H_a} = pK_a + \log(BHCO_3)_a - \log(H_2CO_3)_a,$$

when

$$pK_a = 6.11$$

$$\text{m. eq. } (H_2CO_3)_a = 0.0331\ (H_2O)_a (pCO_2)$$

and

$$(BHCO_3)_a = (\text{total } CO_2)_a - (H_2CO_3)_a.$$

The base bound by protein was calculated according to the method of Van Slyke, Hastings, Hiller and Sendroy.[10]

$$\text{m. eq. } (BP)_a = 0.104\ (P)_a\ (pH_a - 5.08),$$

when

$(P)_a$ = the number of grams of protein per liter of serum.

REPORT OF CASE

History.—It is difficult to state when the patient's illness began. Her biography is in many ways a narration of her symptoms; her illness is her life story. She is white and unmarried.

The patient's mother is a stout woman aged 49, simple and somewhat ignorant, who manages to restrict the patient's activities for the daughter's "own good." The patient's father died in 1931, at the age of 45; according to the patient, he was "cheerful and kind, except when he had been drinking." "His death was caused from heart trouble, gastritis and a fall that caused trouble in his chest." In 1934 a stepfather joined the household. He is rather severe and has a temper. The patient has three brothers. A paternal aunt and a paternal uncle have dementia paralytica.

The patient was born in 1915. According to the patient, birth was difficult because she had "growed to her mother." According to the mother, the birth was normal; the child was breast fed, and "there was a long time before she talked." At the age of 2 months she had whooping cough. At the age of 1½ years, according to the mother, the patient "fell into a cesspool, feet first; little brother saw her; she kind of lost her breath, was gasping; then she had convulsions two days after that, during which she would stiffen out for five or ten minutes; she was put into hot water to relieve them." According to the patient, "it turned into pneumonia. For six weeks I laid between life and death." At the age of 6 "I had measles and thought it terrible, as I was kept in a dark room."

The next year the patient started school. She had frequent colds and otitis media. She was not completely free from pain in the ears for a long time after this. Biting the nails was noted at this time. The patient remembers this part of her life as fairly pleasant. It was mixed with picnics and trips to the beach.

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9. Bock, A. V.; Dill, D. B.; Edwards, H. T.; Henderson, L. J., and Talbott, J. H.: On the Partial Pressure of Oxygen and Carbon Dioxide in Arterial Blood and Alveolar Air, J. Physiol. **68**:278, 1929.

10. Van Slyke, D. D.; Hastings, A. B.; Hiller, A., and Sendroy, J., Jr.: Studies of Gas and Electrolyte Equilibria in Blood: XIV. The Amounts of Alkali Bound by Serum Albumin and Globulin, J. Biol. Chem. **79**:769, 1928.

In the third grade she missed two months of work because of a broken arm. Another brother was born. The mother remembers that the patient walked and talked in her sleep. At the age of 11 the menstrual periods commenced; the onset was relatively uneventful, although the patient remembers feelings of strangling about this time.

In the following year many minor accidents occurred, over which much fuss was made. After falling on her knee, she "went on crutches for a whole summer" and "had electric treatments for about a year"; she also "kept throwing her back and hip out."

In the same year another incident occurred. The patient, speaking of sexual matters, reported: "They say I'm old fashioned. I don't believe in any such actions, unless married or engaged." She then continued: "I was forced once, at the age of 12. It was a married man. I despise him. . . It hurt plenty, so much that I don't want it again. That queered me in the beginning." The patient never told her mother or father of this incident. She was afraid that they would blame her, and, in addition, she feared what her father's temper in a drunken mood might lead him to do.

The patient continued in school and, except for occasional trouble with her ears and knees, was in fairly good health. School was somewhat difficult, although she did not do badly. She said that she studied hard, and needed to because she was a "blockhead." At 15 she fell and hurt her knee again; she was "on crutches for a few months and had electrical treatments twice a week." The next year two minor accidents occurred, and she kept her arm bandaged for more than three months. A dog bit her "right on the place where the burn had been."

The next year, "while studying my home lessons one night, my folks heard a scream, came and found me laying on the floor in a dead faint. I was put to bed and had to remain there for a month or so." Shortly after this the father came home drunk and pressed her to him; the patient thought he was trying to be too affectionate and was very much frightened. Two months later he became ill and died; he did not want to see the daughter at his bedside.

The same year Mrs. X came into the patient's life. Both were members of a special religious group and met first at a revival meeting. The following year the patient's mother remarried. At the same time, she stated, on the way home from school she was again violated, this time by two high school boys. Tonsillectomy, appendectomy, German measles, trouble in the ears, legs and knees and a long period on crutches were her fate this year. The patient had stopped school by this time. The lessons had been more difficult; her grades were bad, and her absences had increased.

She worked at various jobs. She received $4 or $5 a week, worked for relatives for room and board and took care of her sick grandmother. About this time there was an attack of which the patient said: "I don't remember how it came on, but I was twitching all over, had a fever and was unable to eat or sleep much. My right side got so I couldn't move it. My face drew down on that side; my eyes went blind, and I was unable to see for about three or four weeks, when one eye gradually came back, then the other. My head had feelings I am unable to describe. At times I didn't know what went on." Later, "I was eating and sleeping poorly and had pains all over my body."

In the meantime the only pleasant thing that life held for her was her friendship with Mrs. X, whose husband slept with the son while she slept with the patient. "During the night I shook so the whole bed shook. My mother suggested an osteopath. He was an ex-minister and believer in divine healing. He worked on my spine and brought a group from the church to pray over me."

The church members finally persuaded the patient to come to the church for divine healing. She reported this treatment as follows: "It was a wonderful experience. I didn't believe much in it. My friends teased and teased me to go. Ten or fifteen gathered around me, and I sat in a chair; they anointed me with oil, and the minister laid his hand on my forehead. They all prayed; he prayed, and they all prayed afterward; I prayed also. I was lost in prayer; I didn't know whether people were there or not. I was lost in prayer, talking to God. I could see him as plain as I can see you. He has long, wavy hair and a curly mustache and whiskers. He isn't beautiful or handsome, but he is beautiful. He wasn't good looking, but his face would be beautiful. He seemed to have his hand on my head, seemed as if when I walked forward he walked with me, with his hand guiding, and then it was as if he drifted out of sight. I seemed to shake all over for a minute, and there I was standing in front of the people, and I didn't twitch after that."

After this experience the patient worked for a woman who had asthma; coincident with one of her mistress' severe attacks, the patient started to have spells of "panting for breath." "My hands got numb and clenched up; also my feet started to turn at the ankles." The attacks were rare at first but gradually increased in frequency, until she had one every day. "Finally, one Sunday I had it for seven hours and knew nothing of what went on around me." The patient was sent to a hospital. She continued: "There I was given hypodermics and ether when I took spells. At times my back would also double up. My head sometimes got numb, and my eyes closed for a spell; also, my stomach got numb; I was also given calcium and cod liver oil five times a day." The hospital sent her to Dr. Joseph Aub, of the Huntington Memorial Hospital, Boston, who referred her to the Massachusetts General Hospital.

Preliminary Physical and Mental Examination.—On admission, on April 19, 1936, the patient was pale and undernourished. The temperature was 98.6 F., the pulse rate 90; the respiratory rate was 140 and the blood pressure 120 systolic and 60 diastolic. The hands were clenched. The feet were extended and inverted. A slight Chvostek's sign was obtained on the left. The pupils reacted sluggishly to light and in accommodation. The teeth were in poor condition. There was a soft apical systolic murmur. There was slight dorsal scoliosis to the right. The patient looked and acted surprisingly comfortable for a person with such a high respiratory rate; when questioned about her chief complaint, she said: "My ears." Examination of the mental status on admission showed her to be nonchalant about her present condition and extraordinarily dramatic about past events of her life, particularly past symptoms. The mood seemed not unusual, and except for religious ideas there was no unusual preoccupation. Memory was characterized by haziness as to exact dates and sequences. Information was poor, and intelligence seemed low. There was complete lack of insight.

Routine Laboratory Data.—The red cell count was 4,100,000 per cubic millimeter, and the white cell count, 7,150. The Hinton reaction was negative. The stained blood smears and differential white cell count showed nothing unusual. The tests for dextrose, albumin and ketone bodies in the urine gave negative results. There were no abnormal formed elements in the urinary sediment.

Fluoroscopic and roentgen examinations of the chest were reported on as follows: "The diaphragm was low in position, and excursions were limited. The costophrenic angle on the left was obliterated, and there was thickening of the axillary pleura. The pulmonary fields were clear. The cardiac shadow was small and the shape normal. Respirations were extremely rapid. The heart rate was generally

faster than the respiratory rate. At times, however, they were synchronous for from six to seven beats." The electrocardiogram was interpreted as normal.

Course.—Shortly after admission, the patient was given carbon dioxide to breathe; her response was variable. Sometimes she opened her hands completely; sometimes she opened them partially; at other times she would not open them at all. It seemed that part of her behavior depended on the suggestions that accompanied the treatment. During one administration of carbon dioxide mild suggestion put the patient into a partial state of hypnosis.[11] This was accidental; advantage was taken of the situation, however, and she was hypnotized completely; it was then found possible by suggestion to make her breathe normally and to open her hands. Hypnosis was tried several times. When the patient was under hypnosis, and was ordered to open the hands, the clenched fists opened immediately, but only to the position of carpal spasm. Breathing had to be restored to normal by suggestion before the hands opened to a normal position. These treatments cured the hyperpnea and tetany, but on May 3 the patient started to twitch. The twitching began on the right side, and there was hemianesthesia on that side. The anesthesia followed posteriorly the curve of the slight scoliosis. The twitching was accentuated by excitement or displeasure.

During her stay in the ward she was a hard and conscientious worker, at times working furiously at occupational therapy and blistering her hands. She wrote verses and made creditable drawings. She was assigned for a time the job of watching two epileptic children who were having frequent seizures; this she did well and with no sign of imitation of their symptoms.

Interviews with her brought out many elaborate stories that could not be substantiated. These had to do with sexual episodes, assaults and rape. She lived in a community where such things occurred, and it is probable that the story of the first rape, at the age of 12, is true. Her religious feelings were in strong conflict with the sexual misdemeanors of her acquaintances, but some of her attacks of hyperpnea were definitely related to erotic thoughts. There was a good deal of repressed anger against her mother, and she had fantasies about her dead father. She also talked of her "crushes" on her brother and Mrs. X, and in writing her biography for the doctor she was emotional and "felt a lump in her throat" all the time she was writing about Mrs. X.

Time passed; the patient continued to twitch; hypnosis had not stopped the twitching; interviews and reduction of activity to a routine had been tried, without avail. Finally, it was decided to call in Mrs. X to see the patient. The patient was confident she would be better if she saw Mrs. X. After much evasion, Mrs. X arrived; before she left the patient had stopped twitching. It was learned that Mrs. X had smuggled the faith-healer into the ward, and he had there performed for a second time the miracle of healing the patient. The patient's description of the healing follows:

"Praise God for the healing power! He who heals a sufferer that no man can cure!

"I thank God for the healing touch on Dec. 1, 1930, when I was healed instantly from Saint Vitus' dance, this being an experience never to be forgotten. Again, on Aug. 15, 1936, I was again healed instantly, about 4 o'clock, of the twitching, clenching of the hands and rapid breathing. On Saturday, August

11. It is of interest that the patient fell into a state of hypnosis so easily. Seeligmüller (Therap. d. Gegenw. **75**:286, 1934) wrote that hyperventilation is a definite aid in hypnosis, and Lindemann in a personal communication to the authors also noted this.

15, a dear friend, Mrs. X, came to visit me. We talked for awhile about things that happened since we last saw each other and about the church. Later, Mr. Y, the pastor, came in to see me. The three of us continued to talk on the church and about the days I had spent in the hospital. I then asked Mr. Y, also Mrs. X, if they would pray with me. I sat on the edge of my bed, while Mrs. X and Mr. Y, with hands rested on my knees, knelt and prayed for me. I myself was lost in prayer. During this prayer I heard a whispering close to my ear. Turning, I could see the side view of God's head. He whispered these words to me: 'Believe in me, and I will heal thee.' I then had a hard twitch on my right side and rapid breathing for a minute. This passed away, and, thank God! He had taken away my affliction.

"I then came out of what seemed to be a beautiful dream, but it was real. The only thing I could think of for awhile was the hymn 'Only believe, only believe; all things are possible; only believe.'

"I have not had any trouble since the healing and pray that others may also have the opportunity of feeling God's presence and the touch of His hand. May the Lord grant kind heart and healing hand to the nurses and doctors. I hope always to be faithful in prayer and trust our Lord, Amen."

Subsequent Observations.—The patient was discharged from the hospital on Sept. 16, 1936. She looked around Boston for a job and then went home. She won an argument with her mother for a room of her own. Since that time she has been free from symptoms, except for two episodes of rapid breathing associated with erotic thoughts.

Chemical Observations.—The experimental data are given in the table. The changes in the acid-base balance of the blood are presented graphically in the figure, which is constructed on triaxial coordinate paper according to the method of Shock and Hastings.[12] The arterial pCO_2 of the first sample of blood was 15.8 mm. of mercury. The concentration of plasma bicarbonate was 14.3 milliequivalents per liter, and the p_{H_2}, 7.60. The concentrations of total fixed base and sodium present in the plasma were 149.5 and 138.4 milliequivalents per liter, respectively. The concentration of plasma chloride was 109.8 milliequivalents per liter. This represents an increase of approximately 5 milliequivalents above the average for normal arterial blood, when account is taken of the shift between cells and serum with the change in p_{H_2}. The concentrations of calcium and phosphate in the serum were normal. At the time the blood was taken the respiratory rate was 108 per minute.

On the evening of the first day in the hospital the patient received 2 Gm. of ammonium chloride. On the two following days she received 12 and 6 Gm., respectively. One-half hour after the last ingestion of ammonium chloride, the respiratory rate was 62 per minute, and the second sample of blood was taken.

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12. Shock, N. W., and Hastings, A. B.: Studies of the Acid-Base Balance of the Blood: III. Variations in the Acid-Base Balance of the blood in Normal Individuals, J. Biol. Chem. **104**:585, 1934. In the chart for the acid-base balance of the blood of Shock and Hastings, the lines for "CO_2 Excess" and "CO_2 Deficit" were constructed from the data of Henderson and his associates. The chart shown in this communication covers a greater range, and the original data of Henderson are not adequate. D. B. Dill has supplied us with unpublished observations which were used for the construction of the *CO_2 excess* and *CO_2 deficit* lines in our chart. Their positions are slightly different from those shown by Shock and Hastings. These lines follow, for all essential purposes, a normal carbon dioxide dissociation curve.

Date, 1936	Time	Number of Specimen	Whole Blood: Total CO_2, M. Eq. per Liter	Whole Blood: pCO_2, Mm.	Whole Blood: Total HbO_2, M. Eq. per Liter	Whole Blood: Oxygen Saturation, Percentage	Whole Blood: Cell Volume, Percentage	True Plasma: $(HCO_3)^-$, M. Eq. per Liter	True Plasma: $(Cl)^-$, M. Eq. per Liter	True Plasma: $(HPO_4)^{--}$ + $(H_2PO_4)^-$, M. Eq. per Liter	True Plasma: (Proteinate)$^-$, M. Eq. per Liter	True Plasma: $(Na)^+$, M. Eq. per Liter	True Plasma: $(Ca)^{++}$, M. Eq. per Liter	True Plasma: Total Inorganic Base, M.Eq. per Liter	True Plasma: ϵ Anions, M. Eq. per Liter	True Plasma: p_{H_s}	True Plasma: Non-protein Nitrogen, Mg. per 100 Cc.	Comment: Respiratory Rate per Min.	Comment: Type of Ventilation
April 18	4:00 p.m.	1	11.8	15.8	...	....	40.0	14.3	109.8	2.1	16.7	138.4	4.9	149.5	142.9	7.57	23	108	Hyperventilation
April 20	2:30 p.m.	2	9.4	15.5	8.1	96.4	37.6	10.3	115.8	...	14.9	135.5	...	148.0	141.0	7.44	26	62	Hyperventilation
April 20	4:30 p.m.	3	12.9	27.3	...	....	38.7	14.4	113.8	...	15.2	138.6	...	.....	143.4	7.34	..	20	Normal
April 23	2:10 p.m.	4	15.7	22.6	7.5	97.0	34.5	18.1	111.4	...	14.9	142.8	...	151.3	144.4	7.52	36	132	Hyperventilation
April 23	4:05 p.m.	5	16.5	33.2	7.5	96.9	35.3	18.3	109.8	...	12.9	142.1	...	150.8	141.0	7.35	..	18	Normal
April 28	10:20 a.m.	6	13.9	15.9	8.2	96.9	38.3	15.6	108.4	..	17.9	140.7	...	150.6	141.9	7.61	38	110	Hyperventilation
April 28	11:50 a.m.	7	17.1	27.7	7.9	97.5	38.0	19.7	108.0	...	16.2	141.3	...	.....	143.9	7.46	..	20	Normal
April 28	1:00 p.m.	8	19.0	36.5	8.2	93.2	38.1	21.1	107.8	...	15.5	142.0	...	.....	144.4	7.38	..	18	Normal
May 7	8:30 a.m.	9	19.4	37.0	7.6	96.4	36.6	21.3	106.4	2.8	16.0	138.2	4.4	149.5	146.5	7.37	40	115	Tachypnea

Hypnosis was started immediately. The changes in concentration of several constituents of the blood following ammonium chloride therapy were large. The p_H decreased from 7.57 to 7.44, and the concentration of bicarbonate decreased from 14.3 to 10.3 milliequivalents per liter. The arterial pCO_2 was unchanged. The concentration of total fixed base diminished 1.5 milliequivalents, and that of plasma sodium, about 3 milliequivalents per liter. The concentration of plasma chloride, 115.8 milliequivalents per liter, was the greatest observed during the period of study. The cell volume decreased 2.4 per cent, and plasma proteinate, 1.8 milliequivalents per liter. Ninety minutes after hypnosis was started the patient was relaxed; tetany was gone, and the respiratory rate was less than 20 per minute. She was allowed then to come out of hypnosis and remain quietly on the bed. The respiratory rate did not exceed 16 per minute in the following thirty minutes. At this time the third sample of blood was taken. In this sample the p_H decreased to 7.34, while the bicarbonate concentration returned to 14.4 milliequivalents per liter. The tension of arterial carbon dioxide was 27.3 mm. of mercury. This was about 10 mm. greater than that for the first and second specimens of blood. During the next hour the respiratory rate increased to 100 per minute.

The fourth sample of blood was taken on the afternoon of April 23. In the intervening three days the patient had been ambulatory, and no special treatment had been prescribed. Before the fourth sample was taken the respirations were extremely shallow and the rate was 132 per minute. The variations from normal in the concentrations of the constituents of the blood were not as great as those observed on admission. The bicarbonate concentration was 18.1 milliequivalents per liter; the p_H was 7.52, and the arterial tension of carbon dioxide was 22.6 mm. of mercury. The concentrations of sodium and total fixed base in the plasma were normal. Hypnosis was repeated immediately after this sample was drawn. During the next ninety minutes the respiratory rate returned to normal; the patient was allowed to come out of the hypnosis, and the fifth sample of blood was taken. In the interim the p_H decreased 0.17; the arterial pCO_2 increased 10.6 mm. of mercury, and the concentration of bicarbonate increased 0.2 milliequivalent per liter. The concentrations of chloride and proteinate decreased 1.6 and 2 milliequivalents per liter, respectively. The cell volume, oxygen capacity and concentrations of sodium and total fixed base did not change.

On April 28 the experiment was repeated, and three samples of blood were taken. The first specimen (sample 6) was taken about twenty minutes after hypnosis was started; apparently, the suggestion had not yet taken effect, for the respiratory rate was 104 per minute. The concentrations in the plasma of all the constituents analyzed were similar to those observed on admission. The p_H was 7.61, the most alkaline state observed. The seventh sample of blood was taken seventy minutes later, when the patient was out of hypnosis but suggestion had reduced the respiratory rate to 20 per minute. The patient continued to breathe at a normal rate the rest of the day. The eighth sample of blood was drawn two and one-half hours after the sixth. During this period the p_H decreased from 7.61 to 7.38. The arterial pCO_2 increased from 15.9 to 36.5 mm. of mercury, and the concentration of bicarbonate, from 15.6 to 21.1 milliequivalents per liter. The concentration of chloride decreased 0.6 milliequivalent, and that of sodium, 1.3 milliequivalents per liter. The concentration of proteinate decreased from 17.9 to 15.5 milliequivalents per liter. The cell volume showed little change.

On May 7 the last sample of blood was taken. The respiratory rate was 115 per minute; the respirations were shallow, however, and it was believed that ventilation was approximately normal. The normal concentrations of most con-

stituents of the blood confirmed this impression. The p_{H_2} was 7.37, and the arterial pCO_2 was 37 mm. of mercury. The concentration of bicarbonate was slightly below normal. The concentration of the other constituents was within the range for normal women.

The oxygen saturation of the arterial blood was determined in most samples. Except for the blood taken after hypnosis on April 28, the saturations were all above 96 per cent.

COMMENT

This study of the quantitative changes in the blood which accompany prolonged hyperventilation has yielded pertinent data concerning respiratory alkalosis. As alkalosis develops with rapid breathing the arterial tension of carbon dioxide decreases; carbon dioxide is washed out of the blood, and the p_{H_2} increases. A shift in the acid-base balance of the blood similar to this is observed in physiologic experiments on spontaneous overventilation.[13] The prolonged and excessive character of the hyperventilation in the patient under discussion did not alter the magnitude or the nature of these changes. Further, there is little evidence from our data that the physicochemical equilibrium of the body became intolerant to hyperventilation of such duration. On the contrary, the changes in p_{H_2}, pCO_2 and $(HCO_3)_2$ seven weeks after the onset were similar in magnitude to those seen after two hours of hyperventilation.[14]

The low partial pressures of carbon dioxide in the arterial blood which were observed in this patient are approximately the minimum for human beings. At different times over a period of ten days, this variable was calculated to be less than 16 mm. of mercury in the samples of blood taken before hypnosis. These observations in the hospital and the history of tetany for six weeks before admission allow us to assume that the diminution in pCO_2 was present for several weeks.

The best data on hyperventilation in normal subjects for comparison with these observations are those of Shock and Hastings [13c] at sea level and of Dill, Christensen and Edwards [15] at high altitudes. Utilizing a microtechnic for the collection of blood and determination of the acid-base balance, Shock and Hastings studied the changes as a function of time. In one of their experiments, which was reported in detail, they

13. (*a*) Collip, J. B., and Backus, P. L.: The Effect of Prolonged Hyperpnoea on the Carbon Dioxide Combining Power of the Plasma, the Carbon Dioxide Tension of the Alveolar Air and the Excretion of Acid and Basic Phosphate and Ammonia by the Kidney, Am. J. Physiol. **51**:568, 1920. (*b*) Grant, S. B., and Goldman, H.: A Study of Forced Respiration: Experimental Production of Tetany, ibid. **52**:209, 1920. (*c*) Shock, N. W., and Hastings, A. B.: Studies of the Acid-Base Balance of the Blood: IV. Characterization and Interpretation of Displacement of the Acid-Base Balance, J. Biol. Chem. **112**:239, 1935.

14. Davies, H. W.; Haldane, J. B. S., and Kennaway, E.: Experiments on the Regulation of the Blood's Alkalinity, J. Physiol. **54**:32, 1920.

15. Dill, D. B.; Christensen, E. H., and Edwards, H. T.: Gas Equilibria in the Lungs at High Altitudes, Am. J. Physiol. **115**:530, 1936.

observed an arterial pCO_2 of 14 mm. of mercury after twenty-one minutes of hyperventilation. The minimum pCO_2 was maintained less than one minute. The transitory nature of this change stands in contrast to the long duration in our patient. At high altitude association of hyperventilation and diminished atmospheric pressure is responsible for relatively permanent diminution in arterial pCO_2. The highest altitude at which most persons may become acclimated and establish residence is below 20,000 feet (6 kilometers). At 20,100 feet (6.1 kilometers) Dill, Christensen and Edwards reported an average arterial pCO_2 of 24 mm. of mercury for five subjects who had stayed at this altitude for from one to seven days. The minimum tension which they observed was 19.4 mm. of mercury. This change in arterial pCO_2 is probably close to the physiologic limit for diminished atmospheric pressure. It is doubtful if any of the group would have been able to live at a higher altitude for more than a day with a greater diminution in pCO_2. From the preceding data it may be concluded that the relatively permanent and profound diminution in arterial pCO_2 in this patient is a unique observation.

In respiratory alkalosis the diminution in pCO_2 is accompanied by simultaneous diminution in $(HCO_3)_s$. Grant and Goldman [13b] studied this phenomenon in twenty-four experiments on normal subjects and observed a minimum bicarbonate concentration of 16.5 milliequivalents per liter. In five similar experiments Shock and Hastings [13c] observed a minimum concentration of 17.4 milliequivalents per liter. These concentrations are about 2 milliequivalents greater than the minimum observed in the plasma of our patient three days before and five days after the experiment with ammonium chloride. After the ingestion of ammonium chloride, the $(HCO_3)_s$ decreased to 10.3 milliequivalents per liter.

A diminished concentration of plasma bicarbonate may be produced by at least three processes: (1) loss of fixed base, (2) increase in fixed acid and (3) increase in p_{H_s} which allows the protein to combine with additional base, at the expense of bicarbonate. Decrease in concentration of fixed base or increase in concentration of fixed acid produces a demonstrable change in the acid-base balance of the blood. In the graph such a change would be represented by a shift toward *acid excess* or *metabolic acidosis*. If neither of these operations has taken place and the concentration of bicarbonate is decreased because of increased p_{H_s}, the path of the change follows the carbon dioxide dissociation curve. In experimental hyperventilation increase in p_{H_s} is accompanied by diminution in $(HCO_3)_s$ without significant changes in concentration of fixed acid or fixed base. The path of displacement under these conditions follows the carbon dioxide dissociation curve.

The data on the first sample of blood of this patient are typical of respiratory alkalosis, but their position on the triaxial coordinate graph

does not fall on the carbon dioxide dissociation curve. Inspection shows that while the position is represented as being in the direction of CO_2 *deficit* it is, in addition, below this line and is situated toward *acid excess.* One may assume from this evidence that there were changes in concentration of fixed acid or fixed base in the plasma, in addition to the change in p_{H_2} and $(HCO_3)_s$. The experimental observations on the blood confirm this assumption. The concentration of total fixed base in the first sample of blood was in the low range for normal, and the increase in concentration of acids was about 10 milliequivalents per liter, when account is taken of the shift in acids from cells to plasma with change in p_{H_2}. The changes in plasma chloride concentration and undetermined acid contributed equally to this increase.

Certain inferences may be drawn concerning the nature of this undetermined acid. There were no ketone bodies in the specimen of urine examined on admission, and it may be assumed that there was no ketonemia. The concentrations of sulfate and lactate in the plasma were not determined. At high altitude diminished concentration of bicarbonate is not associated with increased concentration of lactate.[16] In experiments on hyperventilation at sea level, however, the increase in concentration of lactate may be 2 or 3 milliequivalents per liter.[17] This may account for the greater portion of the undetermined acid.

There are no extensive data reported concerning movement of fixed base following hyperventilation. In the clinical studies mentioned in the introduction the patients were suffering from encephalitis. In the patient reported here the nervous disorganization was due to more complex processes: Fear and frustration working on a childish personality apparently can disorganize function even more profoundly than the inflammatory lesions in the three cases cited. Experimental and spontaneous hyperventilation in normal subjects is of such short duration that only minimal changes in the concentration of fixed base are observed. Gollwitzer-Meier and Meyer[18] observed diminished concentration of plasma sodium in two of three experiments on hyperventilation. A similar change was noted by Butler[19] during hyperventilation induced by a respirator. In a typical experiment he observed diminution in concentration of serum sodium of approximately 3 milliequivalents per liter after eighty minutes of hyperventilation. At the same time, there was a decrease in the total carbon dioxide of the serum of 10 milli-

16. Edwards, H. T.: Lactic Acid in Rest and Work at High Altitude, Am. J. Physiol. **116**:367, 1936.

17. Bock, A. V.; Dill, D. B., and Edwards, H. T.: Lactic Acid in the Blood of Resting Man, J. Clin. Investigation **11**:775, 1932.

18. Gollwitzer-Meier, K., and Meyer, E. C.: Tetanie-Studien: II. Ueberventilationstetanie, Ztschr. f. d. ges. exper. Med. **40**:70, 1924.

19. Butler, A. M.: Personal communication to the authors.

equivalents per liter. In a total of four experiments, Shock and Hastings [13c] observed a path of displacement which indicated a slight increase in concentration of fixed acid. Minimal increases in calcium concentration following hyperventilation were reported by Grant and Goldman [13b] and Gollwitzer-Meier and Meyer.[18] In our patient the loss of fixed base from the serum after six weeks of hyperventilation was small. It is possible that greater losses had occurred before she was studied, but we have no information concerning this. The concentrations of sodium and fixed base in the serum on admission were in the low normal range. After the ingestion of ammonium chloride the concentrations decreased slightly, but they returned to normal in a few days. No variation from normal was observed in the concentration of serum calcium. It may be concluded that the mild acidosis was produced in the main by increase in concentration of fixed acid and that the loss of fixed base was minimal.

The changes in the acid-base balance of the blood following ingestion of ammonium chloride can be followed best in the figure. In blood sample 2 the concentration of bicarbonate was about 4 milliequivalents less than in sample 1. The arterial pCO_2 was unchanged, while the p_{H_2} decreased to 7.44 milliequivalents. These data indicate that severe acidosis was superimposed on severe respiratory alkalosis. The acidosis was associated with increase in chloride content of about 10 milliequivalents and decrease in the total fixed base of less than 2 milliequivalents per liter. Cessation of hyperventilation following hypnosis (blood sample 3) produced a shift in the acid-base balance along a path parallel to the carbon dioxide dissociation curve. On April 28, the patient having recovered from ingestion of ammonium chloride, blood was drawn during and after a period of hypnosis. The first specimen, sample 6, was taken shortly after hypnosis was started and before there was subjective or objective evidence of its effect. The p_{H_2} was 7.61, and the arterial pCO_2 was 15.9 mm. of mercury. The properties of this and the succeeding two samples of blood indicated that movement along a normal carbon dioxide dissociation curve had occurred in vivo, reaching at the end of two and one-half hours a normal acid-base balance. The increase in $(HCO_3)_s$ of 5.5 milliequivalents was associated with a decrease of 0.6 milliequivalent in the concentration of chloride, a decrease of 2.4 milliequivalents of proteinate and an increase of 1.3 milliequivalents of sodium. The sum of the changes in these three electrolytes accounts for nearly 80 per cent of the changes in bicarbonate concentration.

Evidence was obtained in this study which confirmed the finding of Shock and Hastings [13c] that tetany in hyperventilation is related to the arterial tension of carbon dioxide rather than to the p_{H_2}. At the time sample 2 was taken the patient had carpopedal spasm, and the respiratory rate was 63. In this sample the p_{H_2} was 7.47, and the pCO_2 was 15.5 mm.

of mercury. Eight days later, sample 7 was taken, after the hyperventilation had been stopped under hypnosis and tetany was no longer observed. In this specimen of blood the p_{H_s} was 7.49, and the pCO_2 was 27.7 mm. of mercury. The critical level for tetany in this patient appeared to be slightly below 25 mm. of mercury.

SUMMARY

The acid-base balance of the blood in a patient with hysterical hyperventilation was studied under various experimental conditions. Quantitative data in the study of psychosomatic problems are rare. In this patient the authors were able to control the prolonged hyperventilation by suggestion and thus indicate that the profound changes in the chemical architecture of the blood were due to psychogenic hyperventilation.

During the period of observation the maximum respiratory rate varied from 75 to 140 per minute. The blood which was taken on admission showed changes in arterial pCO_2, plasma bicarbonate and p_{H_s} similar to those observed in respiratory alkalosis in normal subjects. No significant diminution occurred in the concentration of fixed base. There were increased concentrations of fixed and undetermined acid, the sum of which was approximately 10 milliequivalents per liter. These changes suggested that mild acidosis was superimposed on respiratory alkalosis. The acidosis was increased in one experiment after ingestion of ammonium chloride. In two experiments the patient was treated by hypnosis and suggestion. During these experiments the respiratory rate returned to normal, and changes were observed in the acid-base pattern of the blood which were parallel to the normal carbon dioxide dissociation curve. The data from these observations confirm the hypothesis that the principal factor in producing hyperventilation tetany is diminution in pCO_2 and not increase in p_{H_s}.

THE AYALA INDEX

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In 1923 Ayala [1] suggested the rachidian quotient as a means of ready differential diagnosis of an expanding intracranial lesion and other causes of increased intracranial pressure. The amount of drop in pressure after removal of a given amount of spinal fluid apparently differs in cases of tumor of the brain and those of hydrocephalus or serous meningitis. Balduzzi [2] confirmed the value of this index about a year later, and Claude and his co-workers [3] in 1928 added a note on the clinical importance of the quotient. No other extensive studies have attempted to evaluate this relatively simple clinical procedure. Perusal of the neurologic literature of the last ten years shows the occasional use in differential diagnosis of this index by various clinicians.[4] There has been no systematic attempt by English or American investigators to test the value of this clinical procedure. Pollock and Boshes,[5] in a recent paper on cerebrospinal fluid pressure, alluded to its possible clinical value, but did not present their own data. It is significant that many recent writers on clinical neurologic subjects have mentioned the value of the Ayala index but have not presented clinical data to support their opinions. Thus, Paulian [6] referred to the index in his book on tumors of the brain, but did not study its value in any of his 46 cases.

From the Neurological Services of the Mount Sinai, Morrisania and Montefiore Hospitals.

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1. Ayala, G.: Ueber den diagnostischen Wert des Liquordruckes und einer Apparat zu seiner Messung, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:42, 1923.

2. Balduzzi, O.: Evaluation de la pression du liquide céphalo-rachidien dans les méningites séreuses et dans les tumeurs de l'encéphale, Encéphale **19**:83, 1924.

3. Claude, H.; Lamache, A., and Schiff, P.: Valeur de quelques épreuves rachimanométriques au cours de l'hypertension intracranienne, Compt. rend. Soc. de biol. **99**:300, 1928.

4. Marinesco, G.; Sager, O., and Grigoresco, D.: Considerations sur la pathogénie, le diagnostic et le traitement des méningites séreuses, J. de neurol. et de psychiat. **30**:19, 1930.

5. Pollock, L. J., and Boshes, B.: Cerebrospinal Fluid Pressure, Arch. Neurol. & Psychiat. **36**:931 (Nov.) 1936.

6. Paulian, D.: Tumeurs de l'encéphale, Paris, Masson & Cie, 1935.

Brain,[7] in his textbook, also commented on its usefulness, though he did not mention his own experience.

The investigations of Ayala, Balduzzi and Claude and his co-workers were marred by the failure to realize the significance of the amount of fluid removed in relation to the index. In 16 of 27 cases in Ayala's second series,[8] the index was computed after removal of 5 cc. or less of spinal fluid, and in one half of the others, after removal of less than 10 cc. Balduzzi and Claude and his collaborators have been similarly guilty, and thus the clinical importance of their data is vitiated. The reason is readily apparent when one examines the mode of calculating the index.

The Ayala index is usually computed as the product of the final pressure and the amount removed divided by the initial pressure thus: $\frac{\text{Final pressure}}{\text{Initial pressure}} \times$ cubic centimeters of fluid removed = Ayala index. For example, in a case of otitic hydrocephalus, $\frac{250}{300} \times 10 = 8.3$ (high index), and, in a case of an expanding lesion, $\frac{100}{300} \times 10 = 3.3$ (low index). We have found the index of value only in cases in which the initial pressure is above 140 mm. of water. For some reason which we have not yet determined, when the initial pressure is normal or subnormal the Ayala index has been extremely variable and of no aid in diagnosis. The Ayala indexes range usually from 1 to 10 when the amount removed is not more than 10 cc. It is evident that if 5 cc. is removed the maximal index can be only 5, for the ratio between the final and the initial pressure cannot be more than 1, and is usually less. The numerous cases therefore, in which Ayala, Balduzzi and Claude and his collaborators removed only from 3 to 5 cc. cannot be considered in the evaluation of this method. It is also important to mention that if the amount removed is constant, the index represents the ratio between the final and the initial pressure. We prefer to multiply this ratio by 10, because it is easier to deal with whole numbers.

We present the results of our observations on the clinical value of this index, on the basis of an analysis of 186 readings in 181 cases in which cerebrospinal fluid hypertension measuring at least 140 mm. of water was found. In spite of the numerous variables which undoubtedly are present and which influence the magnitude of the spinal fluid pressure and the rate of fall of the pressure as fluid is removed, a large number of cases makes the role of such factors negligible. The results of our observations at the bedside are recorded, and no attempt is made to discuss the interesting and difficult questions of the hydrodynamics of

7. Brain, W. R.: Diseases of the Nervous System, New York, Oxford University Press, 1933, p. 108.

8. Ayala, G.: Die Physiopathologie der Mechanik des Liquor cerebrospinalis und der Rachidialquotient, Monatschr. f. Psychiat. u. Neurol. **58**:65, 1925.

the cerebrospinal fluid involved in the clinical problem. The results of this study are presented in an effort to stimulate interest in this clinical procedure and to urge its wider use. Like any other method of investigation, it is merely an aid and cannot be considered alone, outside the clinical setting in the particular case. It must be evaluated in the light of all the other clinical findings.

Indexes of between 1 and 5 favor the diagnosis of an expanding lesion, such as tumor or abscess. Indexes of between 5 and 6 are equivocal and cannot help in deciding between hydrocephalus or an

TABLE 1.—*Survey of All Cases in Which the Ayala Index Was Calculated*

Distribution of the Ayala Index	Index Above 5.5	Index Below 5	Index from 5 to 5.5
1. Brain tumor (70% below 5, 83% below 5.5)			
(a) Supratentorial	8	29	5
(b) Infratentorial	..	2	1
2. Brain abscess (91% below 5)			
(a) Supratentorial	1	9	..
(b) Infratentorial	..	2	..
3. Subdural hematoma	2	2	2
4. Intracranial aneurysm (100% below 5)	..	2	..
5. Hypertensive vascular disease (87% above 5.5)	36	2	3
6. Hydrocephalus (otitic and sphenoiditic) (80% above 5.5, 100% above 5)	6	..	1
7. Meningitis (82% above 5.5)			
(a) Purulent	4	..	1
(b) Tuberculous	3	1	..
(c) Aseptic	2	..	..
8. Other traumatic conditions, excluding subdural hematoma (83% above 5.5)	10	..	2
9. Postoperative hypertension of the cerebrospinal fluid (63% above 5.5, 91% above 5)	7	1	3
10. Subarachnoid hemorrhage (80% above 5.5)	4	..	1
11. Intracerebral hemorrhage (100% below 5)	..	2	..
12. Cerebromeningeal hemorrhage	3	3	1
13. Syphilis of the central nervous system	1	1	1
14. Miscellaneous grouping	16	2	1
Total number of cases	103	61	22
Total of all cases		186	

expanding lesion. When the index is above 6.5 one is probably not dealing with an expanding lesion.

It is important to give attention to the technic of spinal puncture and of the manometric studies. Ayala performed spinal punctures with the patient in a sitting position. Balduzzi and a few others who used the Ayala index also measured the initial and final pressures with the patient in the sitting position. Claude, Lamache and Schiff [3] suggested that the pressure of the spinal fluid should be taken only with the patient in the lying position. They also warned that the fluid should not be removed too quickly or too slowly and that the initial reading should be taken after a short period, when the excursions of the spinal fluid due to respiratory changes become minimal. In addition, we wish to point out that bending the head forward should be avoided during reading

of the pressure. The line of the head and neck should be on the same plane as that of the vertebral column. The thighs should not be flexed so sharply that they cause abdominal compression. The quantity of spinal fluid removed should be constant—we suggest 10 cc.

The clinical value of this method, in spite of the existence of so many variables, is indicated by the fact that similar indexes have been reported by various observers whose technics unquestionably varied somewhat.

In this report are included 186 consecutive instances of cerebrospinal fluid hypertension (table 1). The only criterion for inclusion of a case was the presence of increased spinal fluid pressure. Cases were excluded in which data were carelessly recorded or in which no more than 5 cc. was removed. A survey of all our cases illustrates the

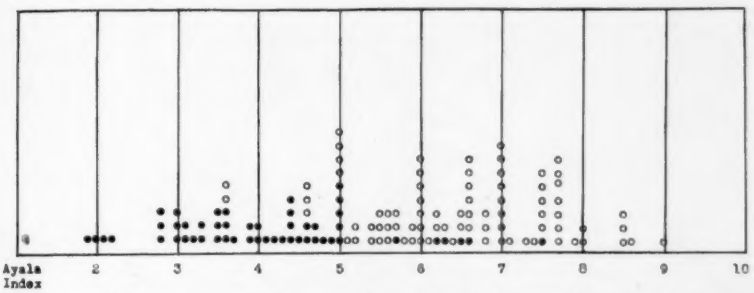

Fig. 1.—Distribution of 130 consecutive Ayala indexes calculated after removal of exactly 10 cc. of spinal fluid. The solid black circles indicate the expanding lesions (51 cases), and the hollow circles, all other conditions (79 cases).

TABLE 2.—*Distribution of Initial Pressures in Series*

Pressure, Mm. of Water	Number of Cases
140-159	14
160-179	22
180-199	26
200-249	55
250-299	26
300-399	25
400-600	18
Total	186

random choice of our material. The miscellaneous group includes a wide variety of conditions.

In figure 1 the results in the first 130 cases, in which exactly 10 cc. of fluid was removed, are presented graphically. Even a superficial examination shows clearly that expanding lesions tend to produce low indexes and all other groups high indexes. Table 2 shows the distribution of the cases according to the magnitude of the initial

pressures. There is difference of opinion as to what is the upper limit of normal cerebrospinal pressure. We have chosen arbitrarily 140 mm. of water, but the data which we present may be analyzed with or without the cases in which pressures were lower.

We have found the index of greatest value in the diagnosis of abscess of the brain, especially in its differentiation from otitic hydrocephalus. The recent interest in otitic hydrocephalus has stimulated search for a more practical method of differentiation from abscess of the brain. Occasionally, as in a case of abscess of the right frontal lobe, focal signs may be minimal, or even absent; this occurred in a case in our series in which the patient was seen early. The Ayala index has been helpful in diagnosis in over 90 per cent of the cases. The results in this series have

TABLE 3.—*Data in Cases of Abscess of Brain*

Case	Location of Abscess	Initial Pressure, Mm. of Water	Ayala Index	Diagnosis Verified	Comment
1. J. G.	Occipital lobe	247	3.3	Yes	
2. P.	Frontal lobe	208	3.7	Yes	
3. M. K.	Cerebellum	208	3.5	Yes	
4. L. H.	Frontal lobe	420	3.6	Yes	Question of encephalitis on clinical grounds
5. G.	Brain stem	280	2.8	Yes	
6. F. P.	Frontal lobe	442	4.9	No	Patient deceased; no autopsy
7. S. R.	Parietal lobe	360	3.0	Yes	
8. H. D.	Cerebellum	280	3.1	Yes	
9. H. A.	Frontal lobe	225	3.5	Yes	
10. S. H.	Frontal lobe	310	3.9	Yes	
11. W. W.	Occipital lobe	170	6.0	Yes	Ruptured abscess with bacterial meningitis
12. S. G.	Frontoparietal lobe	160	4.0	Yes	Multiple metastatic abscesses

been so constant that we have been somewhat concerned, knowing how rarely such perfect correlations are encountered in the analysis of biologic data (table 3).

In case 4 (table 3) an abscess of the frontal lobe was secondary to empyema of the sphenoid sinus. There were no focal signs when one of us saw the patient before admission to the hospital. The Ayala index made us believe that there was an abscess. On the other hand, we shall refer later to a case in which an abscess of the frontal lobe was suspected on the basis of the presence of focal signs. The Ayala index (6) was high. An abscess of the brain was considered unlikely. An autopsy revealed an embolic softening secondary to endocarditis. It is important to point out that the only abscess of the brain associated with a relatively high Ayala index was complicated by terminal bacterial meningitis, with rupture of the abscess into the meningeal spaces. The meningeal response to infection undoubtedly resulted in alteration of the Ayala index, which masked the existence of an expanding lesion.

We wish to compare the findings in table 3, in which the index was above 5 in only 1 case, with those in 7 cases of hydrocephalus, of otitic or sphenoiditic origin (table 4). In almost every case the question of

TABLE 4.—*Data in Cases of Hydrocephalus (Otitic and Sphenoiditic)*

Case	Diagnosis	Initial Pressure, Mm. of Water	Ayala Index	Recovery	Comment
1. M.	Otitic hydrocephalus	372	5.6	Yes	
2. G. M.	Otitic hydrocephalus	285	9.5	Yes	15 cc. removed
3. B. M.	Otitic hydrocephalus	170	5.9	Yes	Petrositis; question of brain abscess
4. P. H.	Sphenoiditic hydrocephalus	190	7.1	Yes	Question of brain abscess
5. M. S.	Sphenoiditic hydrocephalus	160	6.8	Yes	Question of brain tumor
6. B. R.	Otitic hydrocephalus	170	5.5	Yes	Papilledema cleared; encephalogram normal
7. G. D.	Otitic hydrocephalus	165	6.6	Yes	

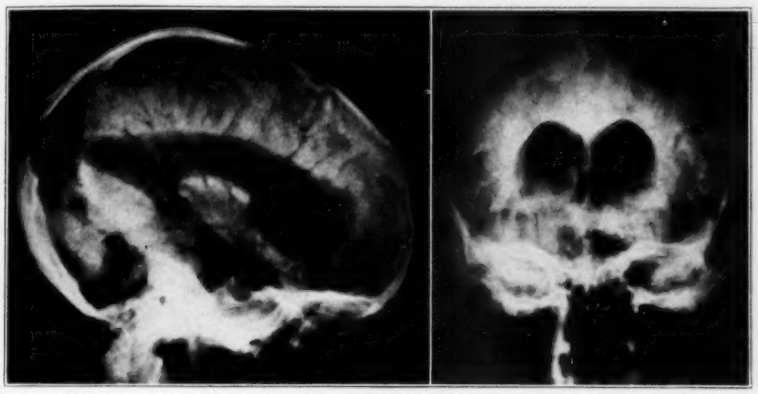

Fig. 2.—Aerograms of the skull.

abscess of the brain was seriously considered, and in a number aerographic studies were made (fig. 2). One can no longer say that the only means of differential diagnosis is aerography. Aerographic studies are not entirely without danger for patients with intracranial suppuration.

We wish to emphasize the importance of case 2 (table 4) in which exploration was about to be made. We urged postponement on the basis of the Ayala index, and the patient made a complete recovery. Case 4 (table 4) is noteworthy. The question of abscess of the brain was seriously considered, and two aerographic studies were made to rule out the possibility. In this case the diagnosis of hydrocephalus accompanying sphenoiditis was made. The diagnosis was not entirely clear, because four days after spheno-ethmoidectomy an infection of the ear (mastoiditis) was discovered. It is possible that the infections of the

ear and sinus were responsible for the hydrocephalus. Carmack [9] and Etienne [10] have already shown that increased intracranial pressure analogous to that encountered in otitic hydrocephalus can occur in association with infection of the sphenoid sinus. In case 5 (table 4) the condition was not complicated by infection of the ear. We suggest the term sphenoiditic hydrocephalus. Goodhart and one of us (N. S.),[11] in a report of case 2 (table 4), commented on the value of the Ayala index in differentiating otitic hydrocephalus and abscess of the brain. Smith [12] reported the same case from the otolaryngologic standpoint.

The analysis of our brain tumor material is interesting and important. In 70 per cent of the cases the index was below 5, and in 83 per cent,

TABLE 5.—*Results of Examination in Eight Cases of Tumor of the Brain Associated with Indexes Above 5.5*

Case	Diagnosis	Ayala Index	Location	Other Disease	Comment
1. B.	Meningioma	10.0	Sphenoid ridge	None	
2. S. H.	Glioma	6.2	Paracentral region	None	Normal encephalogram at time Ayala index was determined
3. P. D.	Meningioma	6.5	Subfrontal region	Hypertension	Hypertension complicated interpretation of Ayala index
4. D. B.	Meningioma	6.3	Subfrontal region implicating chiasm; very large tumor	None	
5. T.	Meningioma	7.5	Parasagittal region	None	
6. G.	Meningioma	6.6	Parasagittal region	None	
7. E. M.	Metastatic hypernephroma	5.7	Metastasis to cranial bone; no intracerebral involvement	Hypertension	
8. H. L.	Metastatic hypernephroma	6.8	Parasagittal region	None	

below 5.4. It is instructive to study the exceptions in this series of tumors of the brain (table 5). These exceptions throw light on the physiologic problems involved. In 6 of 8 cases the tumor was a meningioma; all were extracerebral. One was a glioma, associated with a normal encephalogram. The explanation is clear. A meningioma, in addition to deforming the ventricular system and breaking up the head of pressure, causes accumulation of cerebrospinal fluid by removing extensive surfaces for resorption of spinal fluid. Meningioma some-

9. Carmack, J. W.: The Relation of Increased Intracranial Pressure to Disease in the Pneumatic Spaces, Ann. Otol., Rhin. & Laryng. **52**:364, 1933.

10. Etienne, R.: Symptomes oculaires et orbitaires dans les sinusites sphénoidales, Thesis, Paris, no. 210, 1921, p. 39, case 13.

11. Goodhart, S. P., and Savitsky, N.: Otitic Hydrocephalus, Arch. Neurol. & Psychiat. **32**:1345 (Dec.) 1934.

12. Smith, C. H.: Otitic Hydrocephalus with Report of a Case, Laryngoscope **44**:931, 1934.

times causes hydrocephalus by chronic compression of the venous sinuses. In these cases of meningioma, therefore, there coexisted two factors affecting the cerebrospinal fluid pressure, one tending to give a high, and the other a low, Ayala index. The resultant values, of course, depend on the role of each factor in the particular case. We had in our series an instance of meningioma in which the Ayala index was low, but here the tumor was so large that it caused marked deformation of the ventricular system. In the only case of glioma in the series the encephalogram was normal.

It is also important to point out that the Ayala index is of no value in the diagnosis of tumor after operation. The indexes in the postoperative series (table 6) were almost all high; when preoperative indexes were available they were always relatively low. The operation causes a rapid increase in the amount of spinal fluid—a sort of meningeal

TABLE 6.—*Cases of Postoperative Cerebrospinal Fluid Hypertension*

Case	Preoperative Pressure, Mm. of Water	Postoperative Pressure, Mm. of Water	Ayala Index	Comment
1. O. K.	100	190	7.1	Removal of calcified lobe
2. R. V.	...	400	5.2	Decompression
3. A. C.	...	240	6.0	Angioma of frontal lobe
4. E. H.	130	264	7.5	Preoperative Ayala index 4.6; cerebellar tumor
5. W. Z.	112	350	7.5	No tumor seen at necropsy; basilar arachnoiditis
6. M. M.	124	440	5.4	Meningioma removed
7. J. D.	520	280	7.9	Preoperative Ayala index 5; spongioblastoma
8. R. D.	450	200	6.0	Preoperative Ayala index 3.6; spongioblastoma
9. R.	...	240	8.7	Astrocytoma of frontal lobe
10. A. K.	260	300	5.3	Preoperative Ayala index 2.5
11. J. T.	110	440	6.4	Exploration revealed no abnormality

dropsy. In most cases the presence of an area of decompression after operation alters the entire situation on which the index depends. Finally, the presence of blood in the subarachnoid space calls forth a meningeal reaction, which by itself can cause an elevated index. The index varies also with the time after operation. The rise in the index is pronounced soon after surgical intervention.

Our experiences with the Ayala index in cases of injury to the head were illuminating. We had only a few cases of subdural hematoma in our series, and conclusions must therefore be postponed. We learned, however, that when the Ayala index is over 7, or even over 6.5, the likelihood of a subdural hematoma is less. Given a patient with an injury to the head who when he presents himself a few weeks later has severe headache, and perhaps even papilledema, a high index is against the diagnosis of subdural hematoma, and conservative measures can be used in the management of the condition. Bolotte and Fribourg-Blanc,[13]

13. Bolotte and Fribourg-Blanc, A.: Un cas de larmes de sang par déséquilibre neuro-végétatif post-commotionnel, Arch. d'opht. **48**:697, 1931.

and Claude and his collaborators, as well as one of us (N. S.) [14] have recorded cases of simple cerebrospinal fluid hypertension or hydrocephalus following injury to the head in which there was a high Ayala index. If as the patient is observed progressive coma sets in or focal signs appear, the Ayala index can be disregarded in the same way as is absence of papilledema, or normal spinal fluid pressure will not deter the clinician from immediate exploratory trephination. Furthermore, it is readily conceivable that a flat parasagittal hematoma may produce hydrocephalus in a manner similar to that of a meningioma. It may, early in the history, produce a high Ayala index. When a hematoma of this type becomes so large as markedly to deform the brain, a low index may be expected. If, in addition to the formation of hematoma, there has been subarachnoid bleeding, the additional factor may lead to a high index. Labry and Aufrère [15] reported a case of subdural hematoma in which there were xanthochromic spinal fluid and an elevated Ayala index. Poncet,[16] on the other hand, reported a case in which there were a high index and clear spinal fluid. He removed 20 cc., so that his results are not comparable. Vercelli and Ferrèro [17] removed 35 cc., with no drop in pressure. These random examples indicate the need for standardizing the technic before conclusions can be drawn as to the value of the method.

Our studies on increased spinal fluid pressure in cases of hypertension and hypertensive vascular disease will be reported elsewhere in greater detail. In 87 per cent of 41 cases of hypertensive vascular disease, the Ayala index was above 5.5. In almost none of these cases were there focal signs, and the patients were not admitted as presenting neuropsychiatric problems. They were studied in the medical services of the hospitals. The Ayala index is of especial value in such cases, for occasionally an expanding lesion coexists with hypertensive vascular disease. We have found that when the Ayala index is low, especially below 5, one is justified in postulating the probability of existence of a tumor of the brain with hypertensive vascular disease.

We can illustrate the value of the index by citing the case of a man aged 58 who was brought into the hospital in a state of coma, with left hemiplegia. There was a history of hypertension for thirteen years. One week before admission, while moderately intoxicated, he slipped and struck the left side of his head against

14. Savitsky, N.: Further Comments on Head Injury—the Post-Concussion Syndrome, New York State J. Med. **34**:909 (Nov. 1) 1934.

15. Labry, R., and Aufrère, R.: Hémorragie intradurale localisée post-traumatique. Trépanation. Guérison, Lyon méd. **149**:582 (May 8) 1932.

16. Poncet, J. A.: Compression cérébrale par hématome localisé, Rev. méd. de la Suisse Rom. **55**:522 (June 25) 1935.

17. Vercelli, G., and Ferrero, V.: Sindrome confusionale acuta, manifestazione tardiva di un ematoma fronto-temporale destro post-traumatico, Boll. e mem. Soc. piemontese di chir. **3**:701, 1933.

an iron bar in his bicycle repair shop. Though the blood pressure was 220 systolic and 120 diastolic, the Ayala index of 2.9 made the resident on the neurologic service suspect that there was a coexisting expanding lesion; a subdural hematoma was evacuated on the day after admission.

Another case was that of a man aged 70 who was admitted to the Mount Sinai Hospital with hypertension, hemiparesis and hemianopia. The history was not clear. There was difference of opinion as to whether the papilledema observed in this case was due to vascular disease. The spinal fluid pressure was 600 mm. of water. The Ayala index was 3.04. We have never encountered such a low index in a case of cerebrovascular disease alone. A concomitant tumor of the brain was suspected. A glioma in the parieto-occipital region, in addition to the cerebrovascular disease, was observed. A number of similar instances could be cited.

We have not found any other systematic study of the Ayala index in cases of arterial hypertension. The occasional record of an index which we have encountered in cases reported under other titles confirms our observations that a high Ayala index is found in cases of uncomplicated arterial hypertension associated with increased spinal fluid pressure (Fiamberti [18]). Kiewe [19] reported a case in which the index was 7.7, though he removed 15 cc. of fluid. Fiamberti commented on the high Ayala index. Kiewe merely recorded the initial and final pressures after removal of 15 cc. of spinal fluid.

Analysis of our cases of miscellaneous conditions (table 7) reveals a few interesting points. Some elevations in pressure, such as those associated with multiple sclerosis and Friedreich's ataxia, are not clear. It is possible that the initial spinal pressure recorded in such cases is the "normal pressure." The reading may be due to an error in technic. If a patient is straining, emotionally upset or in marked pain or if the head is bent, the Ayala index will become higher rather than lower.

Case 1 (table 7) is of unusual interest. A woman aged 30, in the eighth month of pregnancy, was admitted to the hospital with bilateral papilledema and the history of a recent convulsive seizure. The blood pressure was normal. Examination of the urine gave normal results. The Ayala index was 6.6; a diagnosis of hydrocephalus accompanying pregnancy was made and conservative therapy advised. The papilledema receded with repeated lumbar punctures. This case probably belongs to those of hydrocephalus accompanying pregnancy described by Schaeffer [20] and Bollack and Salgo.[21] A low Ayala index in a case of this type would have made us suspect a coincidental intracranial neoplasm. No aerograms were made. The patient is well today, more than two years after her admission.

In case 9 (table 7) a woman aged 35 had had continued fever for three weeks and had begun to show severe mental changes. A blood culture showed no growth.

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18. Fiamberti, A. M.: Spasmo retinico, prodromo di accesso maniacale, Riv. oto-neuro-oftal. **13**:608, 1934.

19. Kiewe, P.: Ueber Retinitis proliferans und intrakraniellen Hochdruck, Schweiz. Arch. f. Neurol. u. Psychiat. **35**:42, 1935.

20. Schaeffer, H.: Stase papillaire gravidique avec syndrome d'hypertension intra-cranienne, Rev. neurol. **1**:325, 1932.

21. Bollack, J., and Salgo, N.: Oedème papillaire au cours de la grossesse guéri par la ponction lombaire, Rev. d'oto-neuro-opht. **9**:161, 1931.

She then presented weakness of the right lower part of the face. On the next day she became aphasic, and on the third day she had complete hemiplegia. The question of abscess of the brain was seriously considered. On lumbar puncture the initial pressure was 160 mm. of water, and the Ayala index, 6. This relatively high index was, in our opinion, much against a diagnosis of abscess of the brain, and this opinion was corroborated by a number of other factors, especially the absence of pleocytosis in the spinal fluid soon after onset of the mental changes. Autopsy revealed extensive softening due to embolization from malignant endocarditis.

Cases 11 and 12 (table 7) illustrate the effect of venous resistance on the spinal fluid pressure. In such situations the decreased resorption leads to excessive accumulations of spinal fluid, with communicating hydrocephalus. Porot [22] reported 3 similar cases in which the Ayala index was high.

TABLE 7.—*Data in Cases of Miscellaneous Grouping*

Case	Diagnosis	Ayala Index	Comment
1. F.	Serous meningopathy	6.6	Papilledema receded; complete recovery
2. F. P.	Toxema of unknown cause	5.9	Patient comatose on admission; complete recovery
3. F. S.	Postpartum eclampsia	7.1	Papilledema; recovery
4. M. C.	Idiopathic epilepsy	6.6	No abnormality seen on exploration
5. B. D.	Degenerative disease of central nervous system	7.7	Craniotomy with biopsy
6. M. F.	Carcinoma of lung	7.7	No cerebral symptoms or signs
7. L. W.	Chronic extradural abscess	5.0	Osteomyelitis of skull
8. T. B.	Chronic intoxication	7.5	
9. A. R.	Bacterial endocarditis	6.0	Question of brain abscess; necropsy showed softening
10. J. S.	Dystonia	7.4	
11. D. G.	Chronic rheumatic heart disease	7.7	Spinal fluid pressure 270 mm. of water; venous pressure 21 cm.
12. M. F.	Adhesive pericardium; heart failure	8.5	Spinal fluid pressure 340 mm.; venous pressure 27 cm.
13. C. L.	Multiple sclerosis	7.3	Reason for elevated initial pressure not apparent
14. E. J.	Multiple sclerosis	8.1	
15. J. K.	Multiple sclerosis	8.2	Initial pressure 160 mm.
16. L. N.	Multiple sclerosis	7.5	Initial pressure 160 mm.
17. T. K.	Friedreich's ataxia	8.3	Initial pressure 180 mm.
18. S. F.	Diabetic polyneuritis	5.0	Initial pressure 160 mm.
19. M. R.	Arachnoidal cyst of posterior fossa	6.0	Initial pressure 200 mm.

A man aged 34 was admitted to the Morrisania Hospital with symptoms of acute mastoiditis. After mastoidectomy bilateral papilledema was noted, but there were few significant focal signs. The presence of bilateral papilledema, with recent infection of the ear, led to the diagnosis of otitic hydrocephalus. The Ayala index of 4, however, was disconcerting. He was operated on one year later, at another hospital, and a subtemporal meningioma was removed.

We have also encountered cases in which the Ayala index was not of much help. In cases of hypertension and marked focal signs, due either to cerebral edema or to intracerebral hemorrhage, there may be enough displacement of the ventricular system to give an index below 5. We encountered a case of this type in which there was arterial hypertension. Though the index was below 4, no tumor was observed at necropsy.

22. Porot, A.: Les fortes hypertensions céphalo-rachidiennes d'origine veineuse. Leur latence. La discordance manométrique et clinique, Rev. neurol. **1**:1173, 1930.

Cases of intracranial hemorrhage in which indexes have been recorded have been grouped as those of the subarachnoid, intracerebral and cerebromeningeal types. In the case of subarachnoid hemorrhage there is rarely marked displacement of the ventricles. There is usually an increased volume of spinal fluid, due to the extravasation and the meningeal response to the bleeding. One would expect elevation of the indexes, and the data confirm the impression. When there are extensive intracerebral hemorrhage and edema associated with acute encephalitis, one really is dealing with an expanding lesion, and a low index is to be expected on theoretic grounds. The index associated with cerebromeningeal hemorrhage depends on the resultant effect of two factors—the presence of the intracerebral hematoma, which lowers the index, and the increase in subarachnoid fluid, which raises it.

In most cases of the meningitides there were high Ayala indexes. In cases of tuberculous meningitis we noted a high Ayala index early in the course, with a low index later. The explanation is apparent, as in this disease the exudate at the base often closes the foramina of Magendie and Luschka, thus breaking up the column of fluid in the manner of an expanding lesion.

No conclusions can be drawn from the meager data on syphilis of the central nervous system and intracranial aneurysm. The indexes in both cases of aneurysm were similar to those of other expanding lesions.

We recommend the wider use of the Ayala index.

SUMMARY

The Ayala index was determined in 186 consecutive cases of increased intracranial pressure. A low index, below 5.5, is considered in favor of an expanding lesion with probable deformation of the ventricular system. A high index is against the diagnosis of obstructive hydrocephalus. This index was found to be of greatest value in the differential diagnosis of abscess of the brain from otitic hydrocephalus. It has also proved of value in the detection of expanding intracranial lesions which occasionally coexist with arterial hypertension and cerebrovascular disease. It is an additional diagnostic method and cannot by itself determine the diagnosis in the particular case. It merits further study.

CONCLUSIONS

1. The Ayala index is a valuable method in differential diagnosis of expanding and nonexpanding intracranial lesions.

2. The Ayala index must be determined uniformly and with special attention to the details of the manometric determinations.

3. We suggest that 10 cc. of fluid be withdrawn in every case.

DISCUSSION

DR. LEWIS J. POLLOCK, Chicago: The Ayala index is a quotient obtained by multiplying the amount of cerebrospinal fluid removed by the resulting pressure and dividing by the initial pressure. It may be obtained in another way by dividing the difference between the initial and the final pressure by the quantity of cerebrospinal fluid removed. These are mathematical treatments of a stress-strain relationship. It was conceived by Ayala that the quotient indicates the relative volume of the ventriculosubarachnoid system.

If one removes a certain amount of fluid from a buret, a certain drop of pressure results. If the buret is one of large diameter, the drop in pressure is small as compared with that in a buret of small diameter, both of which contained equal amounts of fluid originally. In other words, the change in pressure is related to the cross sectional area of the buret, and not to the amount of fluid it contains. Unless the cross sectional area of a container is known and included in the calculations, one obtains only an empirical figure, and no indication of the volume of the container. The quotient obtained in this manner would differ in man when one made measurements in the horizontal, the erect and the head-down positions.

Difference in pressure divided by difference in volume and multiplied by volume gives the bulk modulus. It applies only to masses which are compressible and do not change their shape, such as cubes. This treatment, therefore, is inapplicable in man, since the ventriculosubarachnoid system is enclosed in an irregularly shaped container. Granted that for men of equal weight the original volumes are the same, the quotient would measure only the compressibility of the fluid.

Since the cerebrospinal fluid is enclosed in a rigid container open to atmospheric pressure only through the blood vessels, one may employ a similar quotient, Young's modulus, to determine the elasticity of the blood vessels and dura. Here, however, it is necessary to know the area of the enclosing elastic membrane before such a modulus can be calculated.

Given two cylinders closed at one end by rubber membranes, one having a diameter of 25 mm. and the other a diameter of 42 mm., both containing 130 cc. of fluid, if a similar amount of fluid is removed from each the Ayala indexes differ, being 5.2 for the 42 mm. cylinder and 57.2 for the 25 mm. cylinder. This is due to the fact that one is measuring the amount of deformation or thrust of the rubber membranes, which is related to their areas and not to the volumes of fluid contained in the cylinders. Therefore, unless one knows the area of the blood vessels and dura, one again obtains only an empirical figure.

It cannot be denied that an empirical figure such as the Ayala index may be of clinical value. This can be ascertained only if every investigator uses exactly the same technic and mathematical treatment of this measurement. The bore of the needle and the position of the patient must be the same in each case. A manometer giving absolute pressures, not an open one giving relative pressures, must be used, since with initial high pressures the relative pressures drop disproportionately when small amounts of fluid are removed. For the same reason, similar initial pressures must be produced in each case, since even in a system of models with different initial pressures different indexes result when similar amounts of fluid are removed. To my knowledge, these conditions have not been met, and the figures obtained are not comparable.

DR. ISRAEL STRAUSS, New York: I purposely requested that I follow Dr. Pollock in the discussion of this paper. Remembering the paper which he read and published regarding the Ayala index, I knew that he would be able to show scientifically that nothing is known about the Ayala index from the physical

standpoint. As he has just pointed out, it is impossible to explain the Ayala index, or at least to find a physical basis for it. As he said, however, it is possible empirically to use this method in diagnosis, even though one does not understand the mechanism. That is what my associates have done in the cases described.

Dr. Pollock rightly emphasizes an important point, namely, that if this method is to be used and future investigators and clinicians are to correlate their observations with the work of Dr. Savitsky and Dr. Kessler, they must use the same technic, and they must be careful in its use.

I find frequently that when a physician describes a method it is not long before other physicians criticize and find fault with the method; they do not always explain, however, the slight modifications which they make in the technic, and the reader of their articles is thus at a loss to understand the inconsistencies which appear.

As Dr. Savitsky has shown, it is important that their technic should be followed exactly in employing this method of diagnosis. Their technic does not require a closed manometer system. The open manometer, that which is known as the water manometer, is used. I presume that the majority of neurologists use a glass tube which is calibrated. These glass tubes are generally of about the same size. I think, however, that it is immaterial whether they use a glass tube of the same size or one somewhat larger, provided they follow the other requirements of the technic.

Drs. Savitsky and Kessler have pointed out clearly the value of this method. In their hands, it has been a method of great importance in my service at the Mount Sinai and Morrisania Hospitals. It has at times saved us from advising an operation that was unjustifiable and unnecessary. I think all will admit that sometimes, particularly when there is an extracranial focus of infection, one is at a loss to decide whether or not the symptoms of intracranial pressure are due to an inflammatory lesion, consequent to an outside focal infection. Otitic and sphenoiditic hydrocephalus have been mentioned. The latter term may be strange to most, but a case was encountered in which suppuration in the sphenoid sinus produced all the signs of increased intracranial pressure. The encephalogram showed symmetrical hydrocephalus. This case is unique, since no other case has been noted in the literature in which this association was present.

I should like to repeat that the method is one which in the hands of clinicians who follow the technic prescribed by the writers will be of great diagnostic importance and service. Whether or not one can explain scientifically the Ayala index is at present immaterial, except from an academic point of view.

Dr. Robert Schwab, Boston: I have used this index in about 40 cases; at the beginning of the work in 1931 I was impressed by the difficulty in obtaining a reliable initial pressure. A few drops of fluid are frequently lost with the most expert technic. The width of the column of fluid in the manometer, as Dr. Pollock has shown, influences the absolute pressure. The patient may not be relaxed. In working on this index, it occurred to me that it would be of value to plot on the vertical line the pressure after the removal of each cubic centimeter, and on the horizontal line the number of cubic centimeters that was withdrawn. I did this in about 30 cases and obtained curves which can be extrapolated if it is not expedient to take out 10 cc. of fluid, as is often true in cases of subtentorial lesions when pressures are high. In this way, several readings may be obtained, and it is not necessary to depend on one initial pressure at the beginning, when the patient may not be relaxed or when he may be overbreathing. There are enough points, eight or nine in the series, to give a reliable curve. If this curve is concave,

it corresponds to the low, and if convex to the high, Ayala index. This checks well with the formula used and affords a much more accurate method, without the danger of removing 10 cc. of fluid on each occasion. I think that the method on the whole is useful and that one should continue to use it in cases in which the pressures are not consistent with the neurologic data.

Dr. S. Philip Goodhart, New York: In 1934, in the service at the Morrisania Hospital, my colleagues and I encountered a number of cases in which differential diagnosis of cerebral abscess and other conditions was called for. Symonds had published his thesis on otitic hydrocephalus shortly before this time. The clinical manifestations were often so similar and the pathologic conditions and the treatment so different that we sought every aid in diagnosis. The estimation of the Ayala index, a simple procedure, was of aid in coming to a definite conclusion.

Dr. Savitsky and I reported one of the cases of otitic hydrocephalus, with the details of our observations.

On purely empirical grounds, I can speak of the value of the index in recognition of abscess of the frontal lobe. As has been said, the technic must be uniform and carefully executed; on our service, since 1934, the studies have been made or immediately supervised by Dr. Savitsky. One is justified in regarding this simple procedure only as one that should receive attention and be utilized for its possible value. Personally, I am assured that it merits use in the differential diagnosis of expanding lesions and other causes of increased intracranial pressure.

Dr. Morris M. Kessler: We have not yet examined our material for the Ayala volume index, as mentioned by Dr. Pollock. Possibly at a later date we may be able to show something of significance from that group of data. We have the figures, and all that remains is to calculate the index from them. In obtaining data from human beings, we could not carry out a close scientific approximation to the experiments as performed by Dr. Pollock. We could measure only empirical data; on that basis we have found, I believe, a definite indication for wider clinical use of the Ayala index.

It was not long ago that Dr. Leo Davidoff presented a paper on hydrocephalus before the New York Neurological Society, and in the discussion he asked for a clinical method which might aid one in deciding when not to intervene in cases of otitic hydrocephalus with papilledema. We think that this index supplies well the need for the present.

Dr. Schwab's suggestion that one create a number of graphs of the rate of fall of spinal fluid pressure and use the method of extrapolation for calculation of the index is good. This would permit the removal of a smaller number of cubic centimeters of fluid. However, the accumulation of a large number of graphs would be required before the index obtained by extrapolation is sufficiently accurate to be of benefit.

A NEW SERIES OF ANTICONVULSANT DRUGS TESTED BY EXPERIMENTS ON ANIMALS

H. HOUSTON MERRITT, M.D.

AND

TRACY J. PUTNAM, M.D.

WITH THE TECHNICAL ASSISTANCE OF DOROTHY M. SCHWAB, A.B.

BOSTON

A method for the determination of the convulsive threshold by means of graded electrical stimulation has been described by Spiegel [1] and has been employed for comparing the action of certain drugs. The apparatus used in this investigation represents a simplification of that devised by Spiegel and embodies also the arrangement of electrodes employed by Krasnogorski.[2] A description and diagram have been published.[3]

The point of departure for the investigation was the fact that although phenobarbital is one of the most efficient anticonvulsant drugs in common use, other barbiturates are comparatively ineffective, a fact that is often observed clinically and is strikingly demonstrated by the apparatus employed. For this reason and from certain theoretical considerations,[3] a search was made among phenyl derivatives of the general type of phenobarbital, including phenyl, cresyl and tolyl sulfonates, benzoates, ketones and esters, with such radicals as carbamic, barbituric and malic acid, and hydantoin.

METHOD

Cats were used as experimental animals. The threshold for convulsions was determined by applying increasing intensities of an interrupted current from an electrode placed in the mouth to one on the moistened hair of the occiput. The current was measured by a 0-50 milliammeter in the circuit and was drawn from

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1. Spiegel, E. A.: Quantitative Determination of the Convulsive Reactivity by Electrical Stimulation of the Brain with the Skull Intact, J. Lab. & Clin. Med. **22**:1274 (Sept.) 1937.

2. Krasnogorski, N. I.: Tr. Internat. Physiol. Cong., 1935, p. 213.

3. Putnam, T. J., and Merritt, H. H.: Experimental Determination of the Anticonvulsant Properties of Some Phenyl Derivatives, Science **85**:525 (May 28) 1937.

a potentiometer, across which a 45 volt battery discharged through a commutator which interrupted the circuit eighty times a second. The approximately rectangular current produced by this apparatus appears to be considerably more effective and constant in action than sine wave currents.

For each determination the current was applied for a period of ten seconds, arbitrarily chosen. If no convulsion resulted a stronger current was administered after a wait of at least five minutes. The least amperage of current necessary to produce a convulsion in a given animal at a given time was considered to be an index of the convulsive threshold. For untreated animals and those given ineffective drugs the threshold remained remarkably constant over long periods. For example, cat 11 was carefully tested on eight occasions during sixteen days. The convulsive threshold remained constant at a level of 14 ± 2 milliamperes (fig. 1). In general, the convulsive threshold varied in proportion to the size of the animal, and was usually between 10 and 20 milliamperes in cats weighing from 2 to 3 Kg.

A large number of well known sedatives and hypnotic drugs, as well as a series of entirely new ones, were tested to determine which had the highest anticonvulsive effect with the least narcotic action. The method of testing the drugs

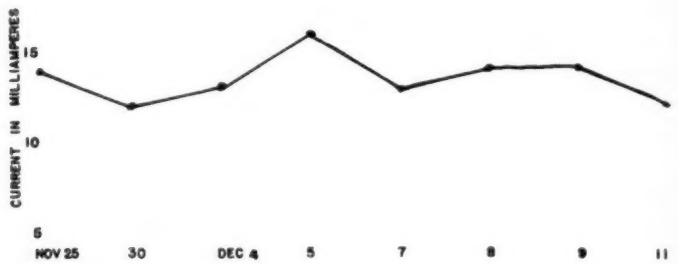

Fig. 1.—Graph illustrating the relative constancy of the convulsive threshold (cat 11, weighing 2.8 Kg.).

was as follows: The convulsive threshold of the animal was always determined immediately before the administration of the drug, and again after an interval of from two and one-half to four hours, to allow for absorption of the drug.

RESULTS

For the sake of convenience, the drugs have been divided into six groups on the basis of our results.

A. Drugs Which Produce Complete Narcosis.—All the drugs tested which produced complete narcosis were effective in raising the convulsive threshold. In most instances it was not possible to produce a convulsion in the narcotized animal by the maximum current which our apparatus produced (from 40 to 60 milliamperes). The drugs in this group which were relatively ineffective in subnarcotic doses were alcohol, sodium iso-amylethyl barbital, iso-amylethyl barbital, pentobarbital sodium, n-phenylethylpropyl barbital, acetophenetidin and phenyl urethane. Two examples are given in table 1.

B. Ineffective Drugs.—A large number of the drugs which were tried were almost or entirely ineffective in raising the convulsive threshold when administered in doses close to the limit of toleration. In testing unknown drugs the amount given was gradually increased until toxic symptoms appeared.

The list of ineffective drugs, with the maximum dose per kilogram, is given in table 2. The results obtained with a few of these drugs are shown in figure 2.

C. Drugs Effective in Non-narcotizing Doses.—Diphenylhydantoin, acetophenone and several phenone and ketone derivatives were the only drugs which in non-narcotizing doses had an anticonvulsive effect com-

TABLE 1.—*Effect of Narcotizing Doses on the Convulsive Threshold*

Cat No.	Weight, Kg.	Date	Time	Current in Milliamperes	Convulsions
7	2.5	Dec. 11	10:29	12	0
			10:35	14	0
			10:45	16	++
			10:47	Iso-amylethyl barbital, 0.1 Gm. by mouth*	
			1:47	Animal very drowsy	
			1:57	20	0
			2:04	30	0
			2:10	40	0
21	4.2	Dec. 11	10:55	15	0
			11:06	17	0
			11:16	19	0
			11:21	22	++
			11:24	Pentobarbital sodium, 0.1 Gm. by mouth†	
			1:20	Cat asleep	
			1:42	24	0
			1:47	30	0
			1:53	36	0
			1:58	45	0

* Iso-amylethyl barbital in doses of 0.05 Gm. produced only a slight increase in the convulsive threshold, although the animal was "drunk."

† Pentobarbital sodium in doses of 0.05 Gm. produced only a slight increase in the convulsive threshold, although the animal was drowsy.

parable with that of phenobarbital. The bromides in non-narcotic doses raised the threshold only moderately (fig. 3).

In table 3 is given the dose per kilogram of the various drugs which prevented the occurrence of convulsions in the cats when stimulated with a full strength current from a 45 volt battery. The results with phenobarbital and diphenylhydantoin are graphically shown in figures 4, 5, 6 and 7.

D. Convulsants.—Several drugs which lowered the threshold. One animal weighing 2.9 Kg. was given a subconvulsive dose (0.75 mg.) of strychnine sulfate. The threshold was lowered from 14 to 4 milliamperes. Another animal, weighing 2.7 Kg., was given 0.5 cc. of pitressin and 170 cc. of water in divided doses during the next hour. The convulsive threshold fell from 20 to 11 milliamperes (fig. 8).

TABLE 2.—*List of Drugs Which Produced Little or No Elevation of the Convulsive Threshold*

Drug	Dose per Kilogram, Gm.	Route of Administration
Acetoxime	0.75	Stomach tube
α-hydroxydiphenyl, sodium salt	0.25	Capsules by mouth
α-hydroxyisobutyric acid	2.00	Stomach tube
Allantoin	0.25	Capsules by mouth
Aminopyrine	0.35	Capsules by mouth
Acetylsalicylic acid	0.30	Capsules by mouth
Atropine sulfate	0.0001	Hypodermic
Benzalacetophenone (benzylidene acetone)	0.25	Capsules by mouth
Benzaldehyde	0.50	Stomach tube
Benzanalide (phenylbenzamide)	0.25	Capsules by mouth
Benzedrine sulfate	0.005	Hypodermic
Benzil (dibenzoyl)	0.125	Capsules by mouth
Benzilic acid	0.125	Capsules by mouth
Borneol (camphyl alcohol)	1.00	Capsules by mouth
Brilliant vital red	2.25*	Intraperitoneal
Bromobutylethylacetylurea (butabral)	0.40	Capsules by mouth
Cinnamylacetophenone	0.125	Capsules by mouth
Dicinnamalacetone	0.50	Capsules by mouth
Dimandelic acid	0.60	Stomach tube
Diphenyl-p-sulfonic acid	0.25	Stomach tube
Diphenyl urethane	0.50	Capsules by mouth
Di(p-methoxy)phenylhydantoin	0.20	Capsules by mouth
Di-p-phenetylurea	0.35	Capsules by mouth
Di-p-tolualacetone	0.50	Capsules by mouth
Di-p-tolylketone	0.50	Capsules by mouth
Ethyldibenzyl malonate	0.45	Stomach tube
Guaiacol benzoate	0.60	Capsules by mouth
Hydantoin	0.20	Capsules by mouth
Hydroxyquinol	0.03	Stomach tube
Indigo carmine	1.5 †	Stomach tube
Iso-amylethyl barbital (allonal)	2	Stomach tube
Methyl-β-naphthylketone	0.3	Capsules by mouth
Methyldiphenylhydantoin	0.37	Capsules by mouth
Methyl-p-tolylketone	0.75	Stomach tube
Naphthalene	0.025	Stomach tube
Naphthalene sulfonate	0.12	Stomach tube
n-benzyl barbital	0.2	Intraperitoneal
n-p-methoxyphenyl barbital	0.03	Intraperitoneal
n-p-ethoxyphenyl barbital	0.025	Intraperitoneal
n-p-tolylbarbital	0.03	Intraperitoneal
o-cresyl-p-toluene sulfonate	0.25	Capsules by mouth
p-bromacetophenone	0.4	Capsules by mouth
p-hydroxypropiophenone	0.3	Capsules by mouth
p-phenylacetophenone	0.2	Capsules by mouth
Phenacyloxyquinoline	0.32	Capsules by mouth
Phenoxyacetic acid	0.3	Stomach tube
Phenylacetic acid	0.5	Capsules by mouth
Phenyl benzoate	0.08	Stomach tube
Phenyl-n-butylketone	0.5	Stomach tube
Phenyl-p-tolylketone	0.3	Capsules by mouth
Physostigmine	0.0005	Hypodermic
Pilocarpine	0.005	Hypodermic
Piperonalacetophenone	0.5	Capsules by mouth
Pitocin	1	Intraperitoneal
Pituitary extract	1	Intraperitoneal
Phenyl salicylate	0.4	Capsules by mouth
Scutellaria	‡	Stomach tube
s-diphenyl urea	0.35	Capsules by mouth
Skatole	0.03	Stomach tube
Sodium m-diphenylbenzene sulfonate	0.2	Stomach tube
Sodium p-diphenylbenzene sulfonate	0.2	Stomach tube
Sodium propiophenone sulfonate	0.25	Stomach tube
Sodium sulfocarbolate	0.3	Stomach tube
Tetramethylammonium bromide	0.15	Stomach tube
Triphenylcarbinol	0.2	Capsules by mouth
Triphenylhydantoin	0.15	Capsules by mouth
Triphenylmethane	0.25	Capsules by mouth

* Given in divided doses over a period of nine days.
† Given in divided doses over a period of six days.
‡ The dose was 25 cc. of a 10 per cent aqueous infusion.

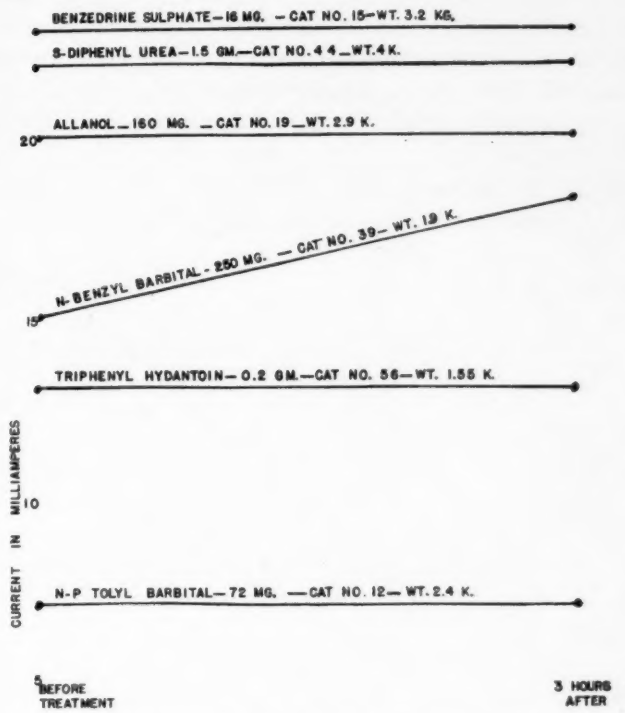

Fig. 2.—Graphs for drugs having no effect on the convulsive threshold.

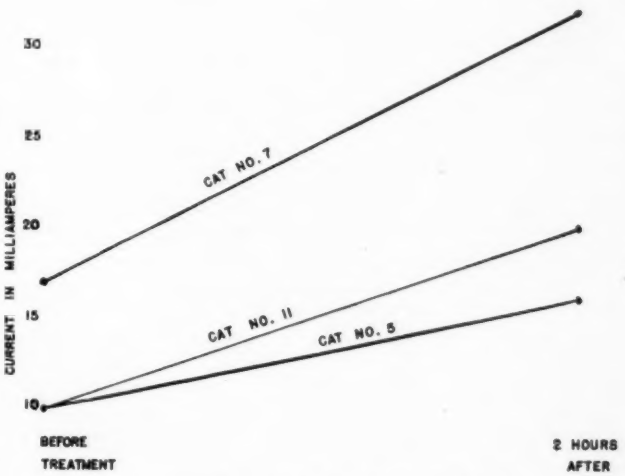

Fig. 3.—Effect on the convulsive threshold of a single dose (1 Gm. per kilogram) of sodium bromide injected intraperitoneally.

E. Carbon Dioxide.—Two cats were put in a covered cage and forced to inhale a mixture of carbon dioxide and oxygen. When the animals showed a marked degree of hyperpnea it was impossible to produce a convulsion with from 30 to 40 milliamperes of current. After the animals had breathed room air for a few minutes the threshold fell again to the normal level.

F. Chronic Experiments.—In addition, chronic experiments were made with phenobarbital, sodium bromide and diphenylhydantoin. In

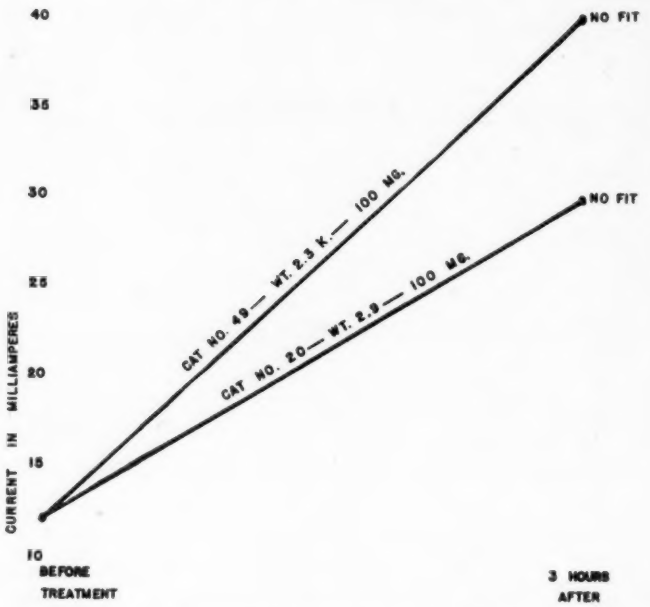

Fig. 4.—Effect on the convulsive threshold of a single dose of phenobarbital given by mouth.

TABLE 3.—*Drugs Which Will Prevent the Occurrence of Convulsions in Animals When Stimulated with Full Strength Current from a 45 Volt Battery*

Drug	Route of Administration	Dose per Kg., Gm.	Condition of Animal
1. Acetophenone	Oral	0.3	Limp, unable to walk
2. Acetophenone oxime	Oral	0.25	Unsteady on feet
3. Benzophenone	Oral	0.3	Limp, unable to walk
4. Diphenylhydantoin	Intraperitoneal	0.025	Slightly "drunk"
5. Diphenylhydantoin	Intravenous	0.015	Slightly "drunk"
6. Diphenylhydantoin	Oral	0.05	Slightly unsteady
7. Phenobarbital	Oral	0.06	"Drunk," unable to stand
8. Phenylglycol	Oral	0.6	Limp, unable to walk
9. Phenyl-n-amylketone	Oral	0.5	"Drunk," unable to stand
10. Phenylpropylketone	Oral	0.75	Limp, unable to walk
11. Propiophenone	Oral	0.2	Slightly unsteady
12. Soluble phenobarbital U. S. P. (sodium phenobarbital)	Subcutaneous	0.033	Slightly "drunk"

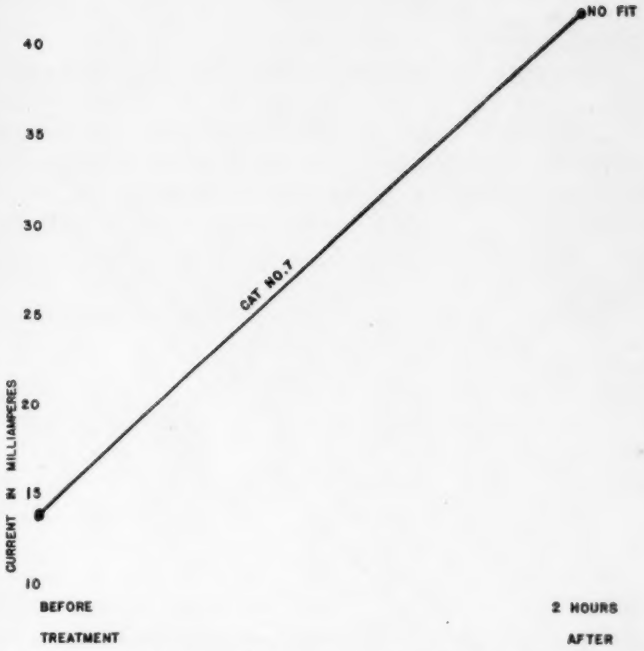

Fig. 5.—Effect on the convulsive threshold of a single dose (20 mg. per kilogram) of soluble phenobarbital U. S. P. (sodium phenobarbital) given intraperitoneally.

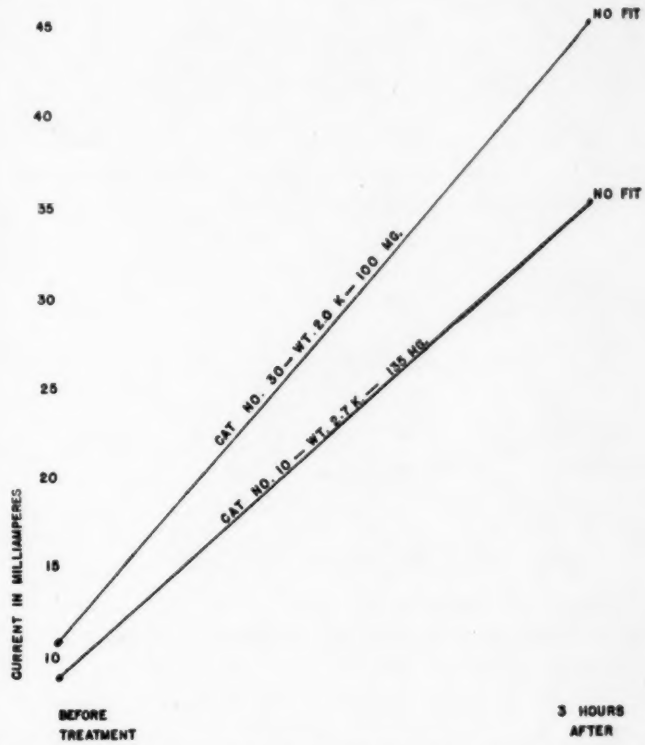

Fig. 6.—Effect on the convulsive threshold of a single dose of diphenylhydantoin given by mouth.

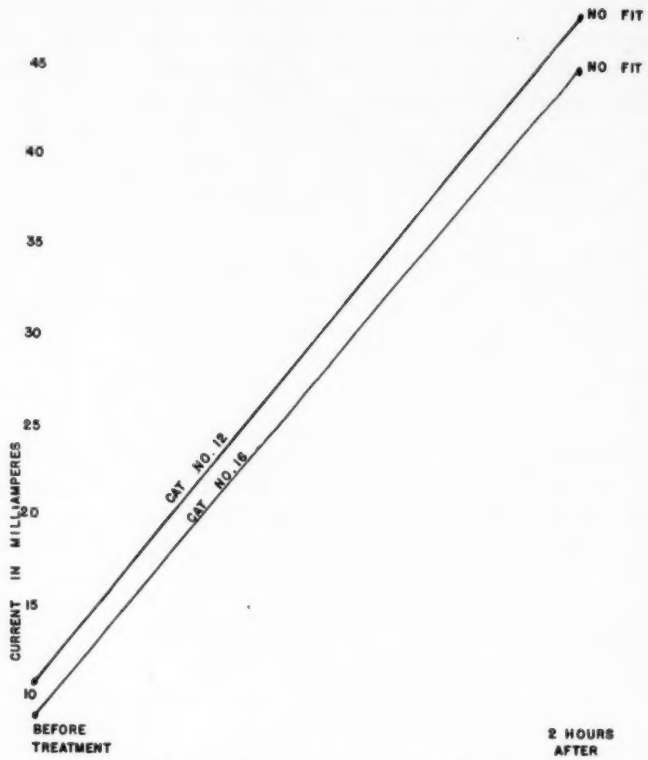

Fig. 7.—Effect on the convulsive threshold of a single dose (20 mg. per kilogram) of diphenylhydantoin given intraperitoneally.

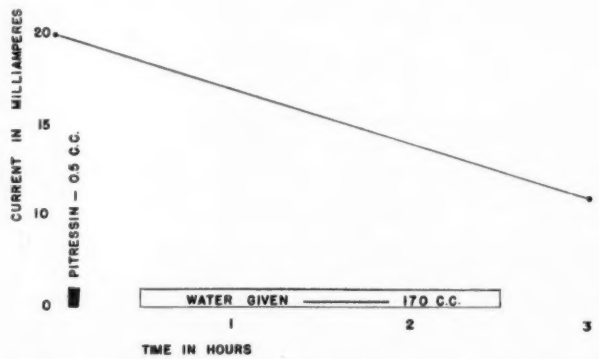

Fig. 8.—Effect on the convulsive threshold of pitressin and ingestion of water (cat 37, weighing 2.7 Kg.).

these experiments animals were given daily doses of the respective drugs, and the convulsive threshold was tested at intervals. There was little change in the threshold with the bromides, although the animals manifested toxic symptoms and eventually died of bromide poisoning (fig. 9). Diphenylhydantoin in doses of from 25 to 40 mg. daily raised the

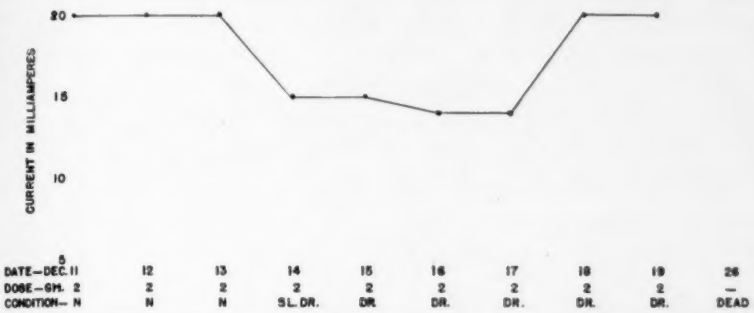

Fig. 9.—Effect on the convulsive threshold of the daily administration of sodium bromide by stomach tube (cat 19, weighing 2.9 Kg.). In this figure and in figures 10 and 11, *N* indicates a normal condition; *SL. Dr.*, slight drowsiness, and *Dr.*, drowsiness.

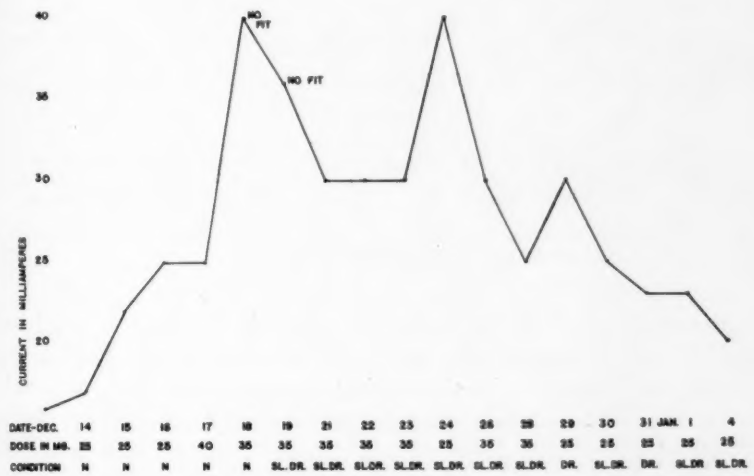

Fig. 10.—Effect on the convulsive threshold of the daily administration of diphenylhydantoin by stomach tube (cat 7, weighing 2.5 Kg.).

animal's threshold until it was impossible to obtain a convulsion. With continuation of the experiment the threshold gradually dropped almost to the original level (fig. 10). The animal was not poisoned by these doses. When phenobarbital was given in doses of 25 mg. daily, the

threshold rose to a level of 34 milliamperes six days after the beginning of the experiment and gradually dropped in two weeks to approximately the original level without producing any serious toxic symptoms in the animal (fig. 11).

COMMENT

The objectives of this investigation were several. First, it was hoped that a reliable and simple experimental method could be devised for the comparison of anticonvulsant drugs, both old and new. The convulsions produced by electrical stimulation appear more closely to imitate the spontaneous grand mal attack than those induced by any other experimental method. Tracings of the electrical activity of the cortex (cortical electrograms) were obtained from our animals by Dr. F. A. Gibbs; the

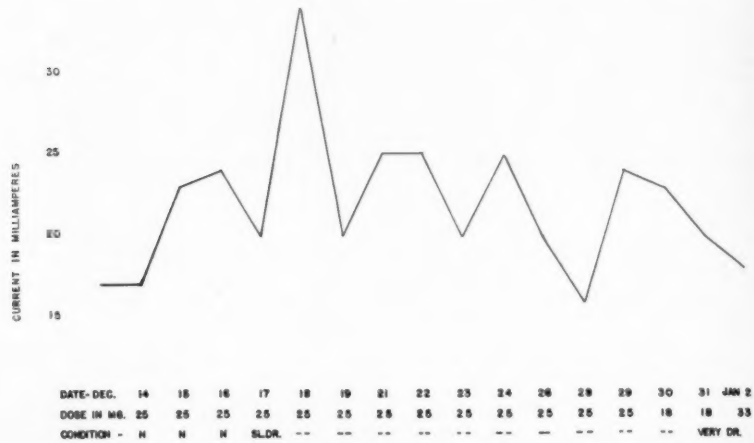

Fig. 11.—Effect on the convulsive threshold of the daily administration of phenobarbital by mouth to cat 10, weighing 2.7 Kg.

disturbance in electrical activity of the cortex in the cats thrown into a convulsion by electrical stimulation is remarkably similar to that occurring in human beings suffering from spontaneous convulsive seizures (fig. 12). The advantages of the constancy of the threshold and the promptness and certainty with which the stimulus can be applied are obvious.

Second, if such a method was devised, it might be used to discover drugs which would have advantages over the standard anticonvulsants. Both the bromides and phenobarbital were first introduced as soporifics and their employment in the treatment of epilepsy was based on clinical trial only. Whether any of the drugs which appear promising under experimental conditions will be of value clinically remains to be seen. Preliminary tests have been encouraging.

Third, it was hoped to learn something of the molecular configurations which are most effective in preventing convulsions. This attempt was not successful. There is an obvious chemical similarity between phenobarbital and diphenylhydantoin, and the acetophenones have linkages in common with the latter drug; on the other hand, many substances containing a similar arrangement are found among the ineffective drugs. There is no reason for believing that the ideal anticonvulsant drug has yet been found, and further search should be made, perhaps also outside the phenyl derivatives.

Fourth, it is conceivable that the method employed may throw light on the physiologic basis and mechanism of human epilepsy. Since the current passes through the whole brain, presumably the portion which has the lowest threshold is that from which the convulsion originates. From the theoretical point of view, the experiments in which the convulsive threshold was lowered are quite as interesting as those in which it was raised.

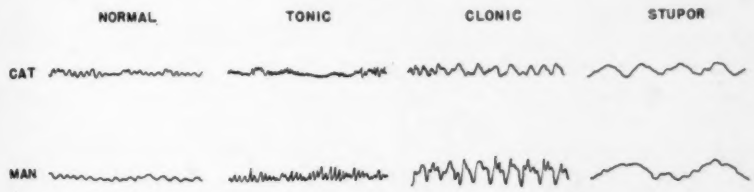

Fig. 12.—Comparison of the cortical electrogram taken during an experimentally induced convulsion in a cat with that obtained during a typical grand mal seizure in man.

The upper tracing in the period marked *tonic* represents the interval during which stimulation was applied to the cat's brain by the method used in this study.

SUMMARY

1. The convulsive threshold of cats was determined by means of an apparatus delivering an interrupted current, measured in milliamperes and graded in intensity, which was passed through the animal's head by electrodes placed on the intact scalp. For untreated animals this threshold was surprisingly constant from day to day.

2. The effect on the convulsive threshold of a large series of drugs, both new and old, was tested.

3. Of the standard drugs, phenobarbital was by far the most effective. Five drugs not previously used as anticonvulsants (diphenylhydantoin, acetophenone, acetophenone oxime, benzophenone and propiophenone) appear to have a greater anticonvulsant effect than phenobarbital, as compared with the lesser soporific effect.

4. Clinical trials of the new preparations are in progress.

DISCUSSION

Dr. William G. Lennox, Boston: Patients with convulsions suffer because the medical profession itself suffers from an attitude of hereditary mental defeatism. By definition, epilepsy is a condition which cannot be helped. Why, therefore, waste time on it? This investigating team was not defeatist in its attitude. It decided that all knowledge concerning anticonvulsant drugs had not died with the originators of bromide and phenobarbital; the results speak for themselves.

This presentation has two aspects: First, and perhaps the most important, is the method of testing anticonvulsant remedies by means of convulsions induced by electrical stimulation. This seems to be a logical method because, as Dr. Gibbs will show in his paper, convulsions themselves are an expression of disturbance in the electrical activity of the brain.

As compared with the use of convulsant drugs, the present method is of value because the convulsion which is thus induced can be more easily stopped. A convulsion induced by a convulsant drug, such as thujone, is like a railroad locomotive, which, once started, is difficult to stop by means of automobile brakes. Electrically induced convulsions can be controlled.

The second aspect of the report concerns the discovery of drugs which may be more useful as anticonvulsants than bromide or phenobarbital. Obviously, the proof of such laboratory work is in clinical trial.

Dr. Ernest A. Spiegel, Philadelphia: I wish to compliment Dr. Putnam and his associates on their excellent results. My co-workers and I have used a similar method for about a year, and Dr. Scala and I showed the apparatus, which consists of a Variac transformer, at the Eighty-Seventh Annual Session of the American Medical Association in Kansas City, in 1936. The current varies in intensity and passes through a relay to the electrodes. The duration of the stimulus can be regulated by the discharge of condensers which close this relay. We can change the intensity as well as the duration of the current and measure the threshold in milliampere seconds.

We applied the electrodes in a different way, namely, to the eyeballs, because the conjunctiva and cornea have low resistances. One has to combat a much higher resistance if one applies the electrode to the skin.

I should like to mention the part of our work which concerns the bromides. We compared the effects of the various bromide salts by injecting equimolecular amounts in rabbits. The effect of sodium bromide and that of magnesium and calcium bromide showed no appreciable difference. It was quite different if we injected ammonium bromide. The threshold curve first rose and then dropped in some animals to the initial level, and sometimes even below it. These effects of ammonium bromide may be due partly to the stimulating effect of the ammonium ion and partly to the acidosis produced by the drug. It was shown by the work of Mishkie that if acidosis is produced the elimination of bromides is facilitated. We tried to combine the administration of sodium bromide with acidosis. The threshold rose less than in the experiments with sodium bromide alone. I mention this particularly because it may explain why it is possible in some animals to obtain very different results with introduction of bromides, depending on the diet and other conditions, and because the ketogenic diet may have some effect on the efficiency of bromide medication.

Dr. Temple Fay, Philadelphia: This is an enlightening advance in the practical means of attacking the problem of the convulsive state. I should like to ask Dr. Merritt and Dr. Putnam if their slide demonstrating the effects of combined forcing of fluids and use of pitressin the results were balanced by any observations on the reduction of fluid or on dehydration. Have they tried insulin

as a convulsant drug? What was the effect of insulin on the convulsive threshold, with and without a program of dehydration?

In Dr. Spiegel's work it has been seen that bromide and chloral change the permeability of the cell membrane and that through the change in permeability these drugs apparently help to raise the threshold and protect the organism.

Dr. Spiegel's work on the delta shows an effect on the physical relationships of the cells as fluid enters, or is denied entrance into, the tissues. His method of inducing the current through the eyeballs rather than through an operative wound removes all doubt as to how much influence direct attack on the cerebral structures may have on the convulsant threshold.

The method of introducing a known amount of current through the eyeballs makes possible repetition of various experiments on the same animal without injury. The authors should be congratulated on this new therapeutic approach to the problem.

Dr. H. A. Riley, New York: I do not wish to discuss the scientific aspects of this presentation, which I thoroughly appreciate, but I should like to call attention to the fact that this association a number of years ago, when it adopted its own nomenclature, banned and omitted the word "epilepsy." I am firmly convinced that nothing, aside from the actual cure of the convulsive state, would detract more from the sum of human misery, as we see it in clinical neurologic practice, than elimination of the word "epilepsy," which carries a connotation to patients and to families which is scarcely equaled by anything but, possibly, the word "cancer." It would contribute greatly to the morale of patients and of their families if physicians would cease using this word. It is convenient, but its effect is devastating on the patient and on his family.

Dr. Tracy J. Putnam, Boston: With regard to Dr. Fay's question: I hope we did not give the impression that the electrodes were applied through an open wound. They were applied one in the mouth and one on the intact skin of the occiput; so no operative procedure was necessary. At the time this work was begun I had heard of Dr. Spiegel's work, though it was not yet in the literature, and also of the studies of Krasnogorski, who used a somewhat similar apparatus for obtaining experimental convulsions. As a matter of fact, we put this particular apparatus together from materials which were immediately available. I must express my thanks to Dr. Hoefer and Dr. Gibbs for excellent suggestions. I think that doubtless many types of electrical stimulation would be equally effective, and perhaps more so. It is our conception that the current passing through the entire cranium stimulates the part of the brain that has the lowest convulsive threshold. I should like to see the same work done with Professor Spiegel's admirable apparatus.

To continue with Dr. Fay's questions: I regret that we did not investigate the effect of dehydration on the convulsive threshold, but that will be on the agendum for this summer; nor have we tried the use of insulin. We were oriented toward drugs of the phenobarbital group, and there are many of them. I think we worked with fifty or more, which entails many experiments, and there are more to come. The substances that we have used may not be the best that could be found. They are simply the best discovered so far; I am sure that other classes of drugs deserve to be investigated.

I should like to emphasize that this procedure appears to initiate a grand mal seizure which is much more typical than the petit mal attack similarly induced. As Drs. Lennox and Gibbs suggest, there seems to be a fundamental difference between the two, and what has been said about these drugs should be taken as applying far more closely to grand mal than to petit mal. We have made a few attempts to use these drugs with patients, with, on the whole, encouraging results.

ASTEREOGNOSIS ASSOCIATED WITH TUMORS IN THE REGION OF THE FORAMEN MAGNUM *

JOSEPH E. RUBINSTEIN, M.D.
NEW YORK

Within the last three years there were observed 2 men, each of whom had an extramedullary tumor protruding through the foramen magnum and definite unilateral astereognosis. The tumor in 1 case was verified by postmortem examination and in the other by operation. In both instances a diagnosis of lesion of the parietal lobe, contralateral to the astereognostic hand, had originally been made by those in charge. The first man had been under observation in the neurologic services of two hospitals for three months, until his death, while the other was studied in a neurosurgical service for one week before the first exploratory cerebral craniotomy, at which nothing abnormal was observed.

By astereognosis I mean loss of ability to recognize by palpation the form of an object, despite the relative intactness of motor power and the primary sensory qualities of touch, temperature and pain. The person with astereognosis is unable to judge or recognize the size, form and consistency of objects placed in his hand unless he looks at them.

The conception that astereognosis is due essentially to a lesion of the parietal lobe is widespread, while relatively little cognizance is taken of the fairly rare observations of lesions of the brain stem and spinal cord as the cause of astereognosis. Mistakes in diagnosis and the resulting delay in proper and timely surgical intervention in cases of lesions of the latter type will continue to occur unless it is realized that astereognosis, even in its so-called pure cortical form, may also occur in association with lesions of parts of the nervous system other than the parietal cortex.

LEADING CONCEPTIONS OF "PURE" CORTICAL ASTEREOGNOSIS

The word "stereognosis" was first used by Hoffmann in 1885 to denote the recognition through palpation of the form of an object in its three dimensions.

Dejerine [1] stated that in no case is there alteration of stereognosis with complete integrity of all other elementary sensations, both super-

Read at a meeting of the New York Neurological Society, Feb. 4, 1936.

1. Dejerine, J.: Sémiologie des affections du système nerveux, ed. 2, Paris, Masson & Cie, 1914, pp. 771-776.

ficial and deep. He asserted that stereognostic perception is an acquisition, due to the evolution of associations of different modes of sensation.

Oppenheim [2] stated that stereognosis is not a sensation by itself but is dependent on the quality of pressure sensation, of passive movements and the position of joints. Since for the recognition of objects by palpation one needs also associative and other psychic phenomena, such as reproduction of memory pictures, it is conceivable that astereognosis is based on disturbances not only of elementary sensations but of cerebral functions.

Head [3] stated that loss of sensation due to cortical lesions is essentially loss of dimensional recognition; i. e., there is loss of localization, two point discrimination, spatial relations and recognition of the size, shape, texture and weight of objects. Stereognosis is most extensively affected by a lesion which involves the postcentral convolution.

Wechsler [4] stated:

> The conception that astereognosis is a purely cortical condition has been assailed on the ground that it is found in peripheral nerve, spinal cord and bulbopontine lesions. This is true, of course, but is obviously due to loss of touch and temperature besides impairment of position sensation and point discrimination. If, however, there is no associated anesthesia, either peripheral or central, astereognosis represents a postcentral, cortical or subcortical (occasionally also thalamic) sensory loss. But in every such case, as Head has shown, position sensation and point discrimination are also impaired.

Bing [5] stated that astereognosis is generally a focal symptom and as such points to the location of the lesion in the middle third of the postcentral convolution, contralateral to the astereognostic hand (see also Bing and Schwartz [6]).

Campora [7] concluded:

> With astereognosis there is always a considerable diminution of tactile discrimination, as detected by Weber's method, as well as that of sense of position. . . . This holds true in diseases of both the central and peripheral nervous system.

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2. Oppenheim, H.: Lehrbuch der Nervenkrankheiten, ed. 7, Berlin, S. Karger, 1923.

3. Head, H.: Sensation and the Cerebral Cortex, in Studies in Neurology, London, Henry Frowde, 1920, vol. 2; reprinted from Sensation and the Cerebral Cortex, Brain **41**:58, 1918.

4. Wechsler, I.: A Text-Book of Clinical Neurology, ed. 3, Philadelphia, W. B. Saunders Company, 1935, pp. 62, 316 and 317.

5. Bing, R.: Compendium of Regional Diagnosis in Affections of the Brain and Spinal Cord, ed. 3, translated by F. S. Arnold, St. Louis, C. V. Mosby Company, 1933.

6. Bing, R., and Schwartz, L.: Contribution à la localization de la stéréoagnosie, Schweiz. Arch. f. Neurol. u. Psychiat. **4**:187, 1919.

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REPORT OF CASES

CASE 1.—*Headaches and numbness of the left hand for five months. Stiffness of the neck, astereognosis and loss of position sense and two point discrimination in the left hand. All other sensations normal. Death twenty-four days following admission, after development of astereognosis in the right hand. Autopsy: cerebrum normal; meningioma wedged in the foramen magnum.*

History.—B. S., a white man aged 58, married, a house painter, was admitted to the Montefiore Hospital on June 3, 1933, complaining of gradual onset of headaches and numbness of the left hand for five months and marked stiffness of the neck for about five weeks. Up to nineteen days before admission he had been studied extensively in the neurologic service at another hospital, where the following prominent objective findings were noted: astereognosis; impairment of sense of position and two point discrimination in the left hand, with preservation of touch, pain, temperature and vibratory sensation; very slight involvement of the cranial nerves, and slight signs referable to the pyramidal tracts, with tenderness to pressure of the posterior cervical muscles on the left side. Encephalographic examination in May 1933 had shown an increased amount of air in the subarachnoid space, with a marked collection of air over the right cerebral cortex. It had been considered, therefore, that the patient was suffering from encephalopathy on a vascular basis, with a focal lesion in the right parietal lobe.

On admission to the Montefiore Hospital nineteen days later, the patient complained that since the encephalographic examination one month previously the stiffness and pain of the neck had increased and that he had completely lost libido. There had been steady progression of the "dead" feeling in the left hand, and the headaches had become severe.

General Examination.—There was marked limitation of movements of the head in all directions because of severe pains in the back of the neck on the left side, with tenderness over the upper cervical portion of the spine and of the deep muscles of the left side of the neck. Pain in that region was aggravated by coughing or sneezing.

Neurologic Examination.—The gait was cautious; the head was kept constantly tilted to the right, and the arms were stiff and held away from the body, with little swinging of the left arm. Examination of the cranial nerves showed slight diminution of corneal sensation on both sides; the right pupil was larger than the left; there were slight ptosis of the left eyelid, hoarseness and some flattening of the left border of the tongue. There was some weakness of the left hand grip and of the muscles at the left elbow; there were no other pareses.

The reflexes were generally hypoactive; the ankle jerk was apparently absent on the left; the abdominal reflexes were unobtainable, and there was impairment of plantar flexion of the big toes.

There was incoordination on the left side. The left extremities showed some ataxia in performing the finger to nose and heel to knee tests, which was most marked with the eyes closed; there were clumsiness in the finger to finger test and dysdiadokokinesis. The right side was normal.

Sensory examination showed that the elementary modalities of sensation were spared; touch and sensation to pinprick were apparently undiminished over the left hand, and the patient could discriminate, equally in the two hands, between temperatures of 28 and 32 C. Position sense was completely lost in the fingers and toes on the left side and was diminished in the left ankle. Vibration sense was diminished in the left hand, and two point discrimination was impaired on the left. There were marked astereognosis and abarognosis on the left side, the patient failing to recognize objects by palpation with the left hand and to discriminate

between hard and soft, round and square and smooth and rough objects, to distinguish different weights and the like.

Laboratory Findings.—Examination of the urine and blood, including serologic tests, gave normal results.

Roentgenograms of the skull revealed nothing abnormal, while those of the spine, in the cervical as well as in the dorsal and the lumbar region, disclosed a moderately advanced degree of hypertrophic spondylitis.

During the patient's stay in the hospital three lumbar punctures were performed. The first showed an initial pressure of 140 mm. of water with faint suspicion of partial block. The second and third punctures showed an initial pressure of 210 mm. of water and a normal reaction to the Queckenstedt test with no evidence of partial block, the dynamics having been checked with amyl nitrite. Examination of the fluid obtained from each lumbar puncture showed slight increase in cells and protein; these changes were explained as due to the recent encephalographic examination (from four to six weeks previously).

Examination of the Fundi.—The ophthalmologist reported that the patient showed "relatively normal myopic fundi."

Clinical Diagnosis.—All observers agreed that the signs and symptoms were due to a degenerative process, probably on a vascular basis, with a focal lesion in the right parietal lobe. The severe pains and stiffness of the neck were said to be a result of the spondylitic changes in the spine with irritation of the nerve roots.

Course.—The patient grew worse. On June 22 he complained of the development for several days of sensations in the right palm similar to those he had had in the left. On June 24 there were definite astereognosis, loss of position sense, pseudoathetoid movements and weakness in the right hand as well as in the left. Early in the morning of June 27 there developed difficulty in breathing and distention of the urinary bladder. Later in the day he became pale and complained of excruciating pain in the neck; the temperature rose to 101 F. He died early that afternoon with signs of medullary failure, associated with vasomotor and respiratory difficulty.

Autopsy.—The brain weighed 1,520 Gm. It appeared to be essentially normal, and internal hydrocephalus was not present. The vessels at the base were normal. A grayish, firm tumor, the size of a walnut, was observed to arise from the meninges at the left of the medulla oblongata. This tumor was pressed against, but not attached to, the substance of the medulla. It was easily shelled out *in toto* from the dural lining of the foramen magnum and the upper cervical portion of the vertebral canal. It protruded for about 1 cm. into the posterior cranial fossa and extended about 2 cm. down the vertebral canal. The left side of the medulla oblongata was flattened and softened. The tumor was attached to the medulla by a few small vessels and by the vertebral artery, which entered the tumor in a hilus-like concavity. Sections at different levels showed marked distortion of the medulla oblongata, which was more pronounced on the left (figs. 1 *A* and *B* and 2). The spinal cord appeared normal.

Microscopic Examination.—There were slight demyelination of the left pyramid and distortion due to compression of the medial lemnisci. The cervical portion of the spinal cord, at a level close to the crossing of the pyramids, showed partial demyelination of the fibers of the posterior columns and of the ventrocerebellar pathways, which was most pronounced on the left. The tumor showed the structure characteristic of a meningeal fibroblastoma (figs. 3 *A* and *B* and 4).

Microscopic Diagnosis.—The diagnosis was meningioma, in the region of the medulla oblongata and the upper cervical portion of the spinal cord.

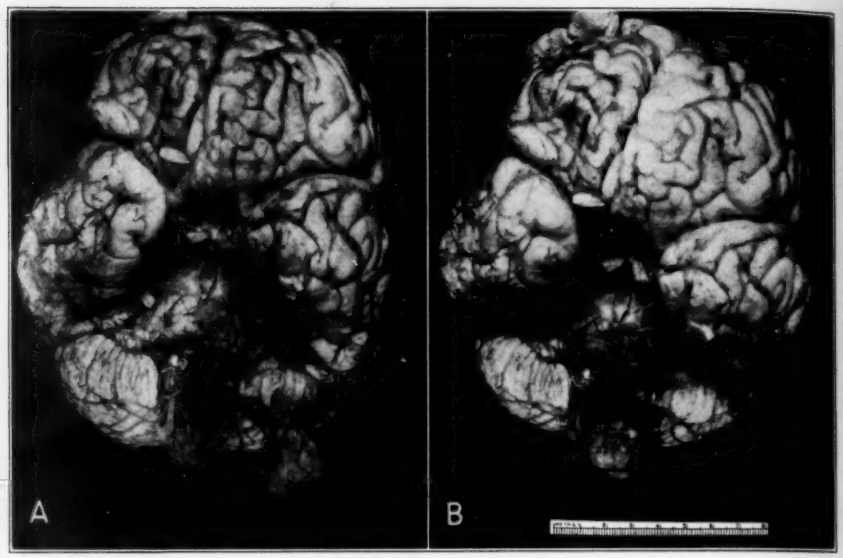

Fig. 1 (case 1).—*A*, attachment of the left vertebral artery to the meningioma, with flattening of the medulla oblongata and uppermost cervical portion of the spinal cord. *B*, meningioma compressing the high cervical region of the cord and part of the medulla oblongata.

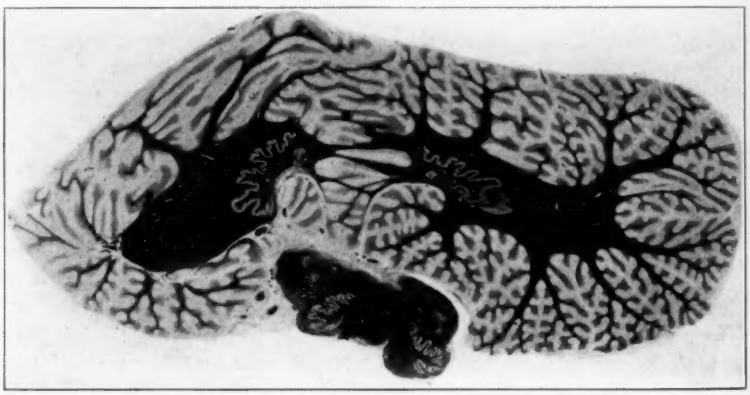

Fig. 2 (case 1).—Distortion of the cerebellum and medulla oblongata by the high cervical meningioma. Myelin sheath stain.

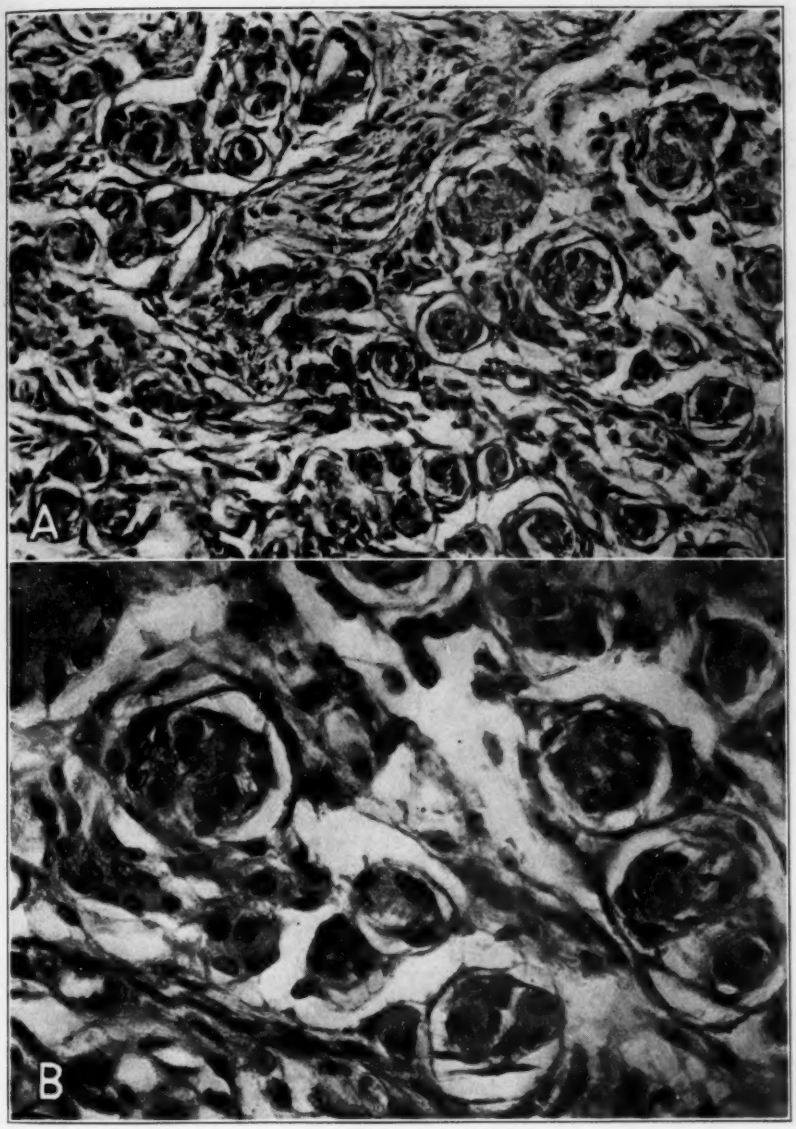

Fig. 3 (case 1).—Typical appearance of a meningeal fibroblastoma with numerous whorls; hematoxylin and eosin stain. *A*, × 100; *B*, × 200.

CASE 2.—*Vomiting for five months; frontal headaches and blurring of vision for three weeks and symptoms of astereognosis in the left hand for one week. Marked bilateral papilledema, with large hemorrhages in both fundi. Normal power and sensation throughout, except for astereognosis in the left hand and slight loss of position sense and two point discrimination. Right temporoparietal craniotomy with cerebral exploration showed nothing abnormal. Ventriculographic examination eight days after operation showed symmetric dilatation of the whole ventricular system. Subsequently, during cerebellar craniotomy a hemangioblastoma in the midline of the cerebellum and protruding down the spinal canal was removed.*

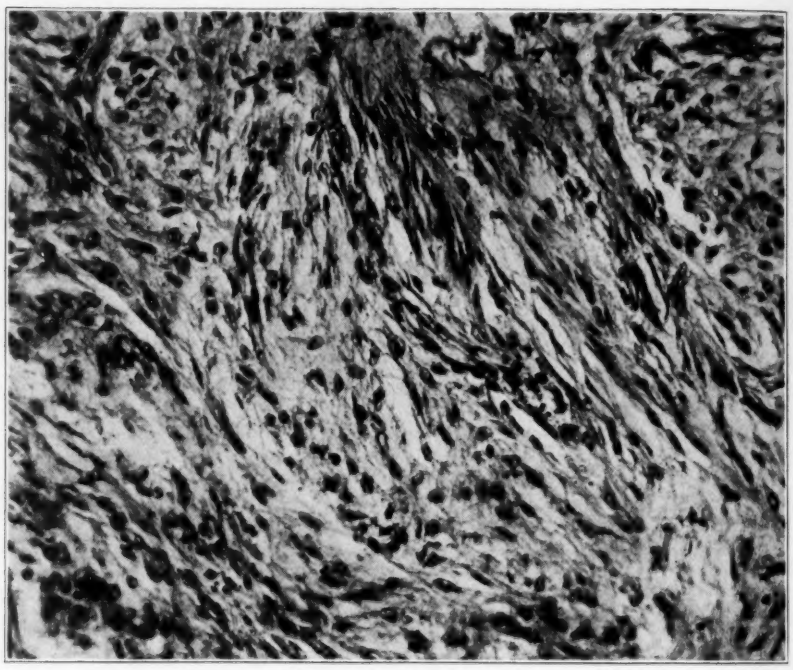

Fig. 4 (case 1).—Palisade arrangement of cells in some parts of the tumor. Hematoxylin and eosin stain; × 100.

History.—R. G. M., a white man aged 29, married, a clerk, was admitted to the Barnes Hospital on Sept. 17, 1934, complaining of vomiting for five months and frontal headaches and dimness of vision for three weeks. The present illness dated back five months, when vomiting with nausea began to occur once or twice a week. He continued, however, to do his usual work. Three weeks before admission there developed right frontal headaches, which became progressively more severe. A few days later there developed dimness of vision in both eyes, and the eyesight diminished rapidly. Three days before admission he was told by this physician that "the eye nerves showed inflammation." On being questioned, he admitted that during the last week he had noticed numbness in the left hand and that in picking up objects he had to look at them in order to identify them, since he could not "feel them well" with that hand.

General Examination.—Physical examination gave essentially normal results.

Neurologic Examination.— The gait and attitude of the head were normal. Vision was poor in both eyes; being 15/40 in the right and 15/30 in the left. The patient could hardly distinguish red from green. There was enlargement of the blindspot in the right eye with a large paracentral scotoma on the nasal side; in the left eye a large temporal paracentral scotoma fused with the blindspot. The peripheral visual fields were normal. There were choking of the disk in each eye, of about 5 diopters, and very large fresh superficial hemorrhages along the veins radiating from the disk and around the macula. All the other cranial nerves were normal.

Power was normal; the dynamometric readings of power in the hands were 85 for the right and 75 for the left (the patient was right handed). There were no signs of incoordination or ataxia, and the reflexes were equally lively on the two sides. Plantar flexion of the big toes was absent, but no definite Babinski sign was elicited.

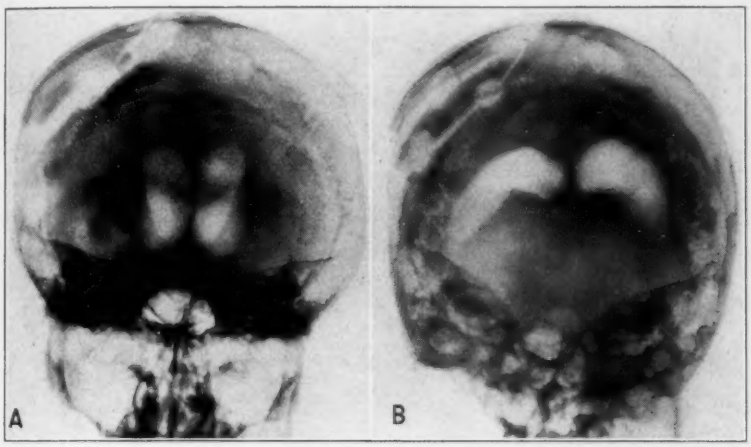

Fig. 5 (case 2).—Uniform dilatation of the ventricular system suggestive of tumor of the posterior fossa. *A*, anteroposterior, and *B*, posteroanterior view.

Sensory examination showed normal sensation throughout to touch, heat and cold and pinprick. Vibratory sensation showed no definite changes. The only evidence of impairment of position sense was the slight pseudoathetoid movement of the fingers of the outstretched left hand. Two point discrimination was slightly diminished on the entire left side, most markedly in the left hand.

There was striking astereognosis on the left side. Common objects, such as a pencil, matchbox, pocket knife, safety pin, towel and drinking glass, were placed alternately in each hand, while the eyes were kept closed. With the left hand the patient was unable by palpation alone to recognize the objects or their form and consistency, and he had a tendency to drop the objects unknowingly from his hand. Stereognosis was normal in the right hand.

The results of laboratory examination of the urine and blood, including serologic tests, were all normal. Spinal puncture was not done.

Roentgenograms of the skull showed prominent convolutional markings in the frontal region.

Clinical Diagnosis.—The diagnosis was a rapidly growing tumor in the right parietal lobe, which apparently started in or near the stereognostic center.

Operation.—A right temporoparietal craniotomy, performed by Dr. Ernest Sachs on September 24 revealed nothing abnormal. There was no evidence of tumor in that region.

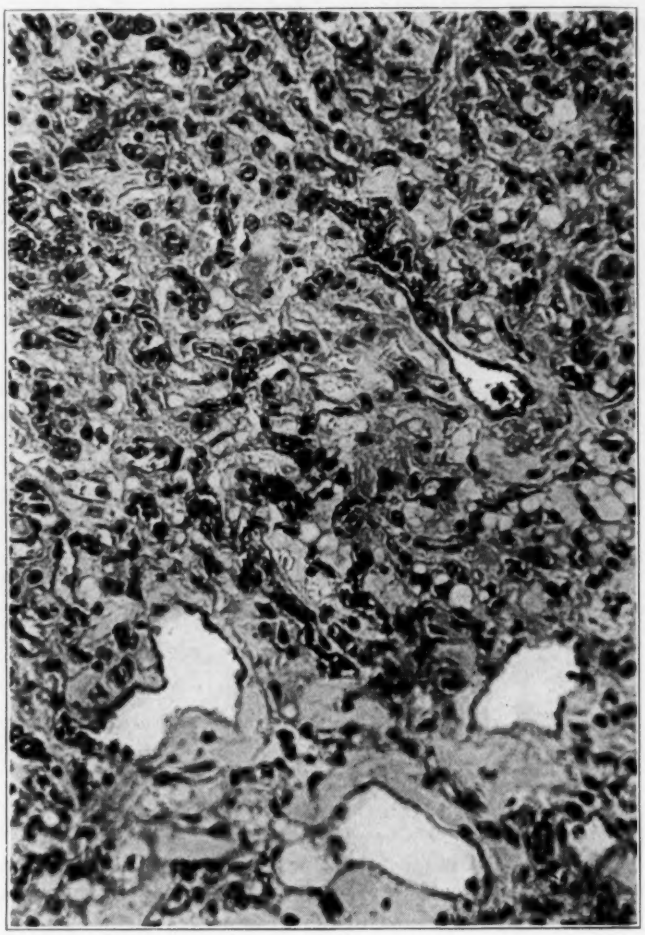

Fig. 6 (case 2).—Hemangioblastoma showing vast number of capillary spaces with markedly proliferated endothelial cells, forming fairly solid tissue. Occasional cavernous vessels are noted. Hematoxylin and eosin stain; × 100.

Ventriculographic examination was performed on October 2. This showed moderate symmetric dilatation of the ventricular system, with the third ventricle apparent in some of the lateral views (fig. 5 *A* and *B*).

Third Operation.—Suboccipital cerebellar craniotomy was performed by Dr. Sachs on October 30. When the basal cistern was opened a tumor was observed

to occupy the midline and extend into the spinal canal. The posterior part of the atlas had to be removed and the dura incised into the spinal canal. The tumor was from 5 to 6 cm. in length and from 3 to 4 mm. across. Large blood vessels entered it. Subtotal excision of the tumor was made with the electric knife, and

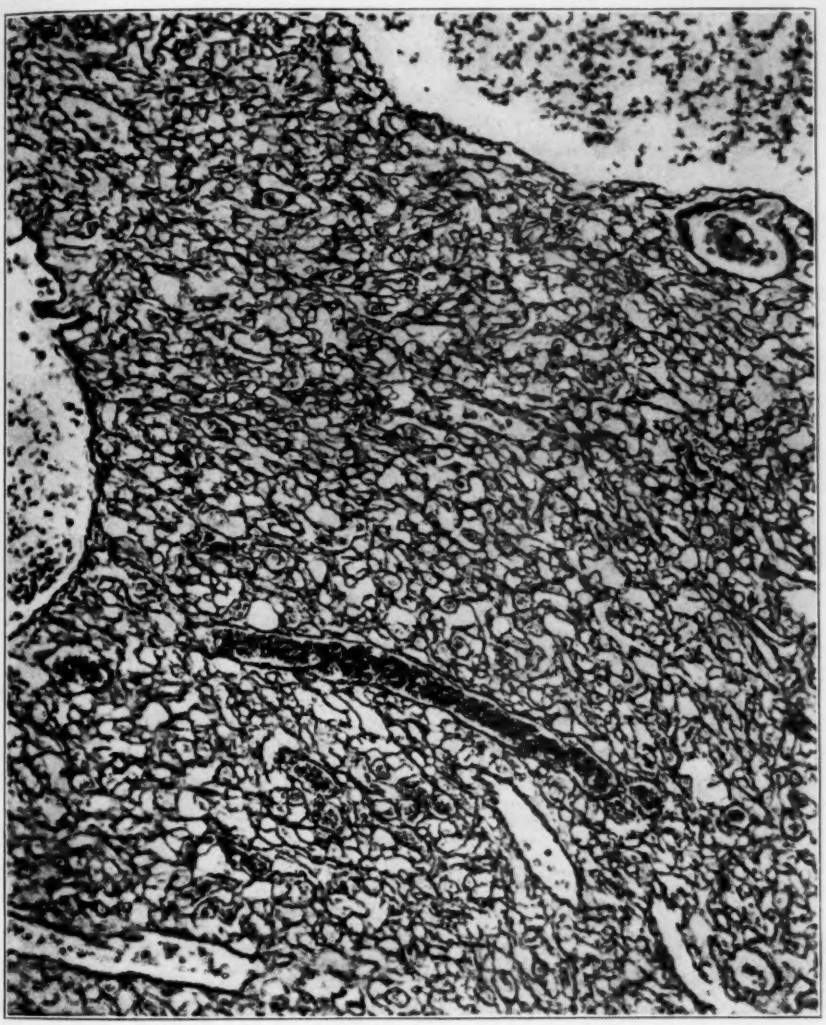

Fig. 7 (case 2).—Characteristic network of reticulin permeating the tumor between the cells. Large cavernous vessels are present. Perdrau stain; × 100.

the part of the tumor which was attached to the medulla oblongata and the floor of the fourth ventricle was left.

Tumor.—Gross examination showed a firm, well encapsulated tumor; it was pinkish yellow and fairly vascular.

Microscopic Examination: Sections showed a moderately cellular tumor consisting of a multitude of capillaries and thin-walled vessels, filled with blood, with cords of neoplastic endothelial cells scattered between the embryonic vessels. Many neoplastic cells were filled with lipoid granules, forming "pseudoxanthomatous" cells. A network of reticulin permeated the tumor (figs. 6 and 7).

Microscopic Diagnosis.—Cerebellar hemangioblastoma, of hemangioendothelial type.

Course.—The temperature remained at about normal level for five days, when there was a sudden rise to 40 C. (104 F.) and signs of bronchopneumonia developed. The patient died two days later. Autopsy was not permitted.

COMMENT

Review of the first case reveals that there were many points which should have led one to believe that the patient had a tumor high in the cervical region of the cord. The constant radicular pain in the distribution of the cervical nerves, the marked stiffness of the neck and the presence of signs of disturbance of the medullary centers should have suggested a pathologic process in that region. However, owing to the fact that astereognosis was a prominent feature in the case, there was the constant tendency to localize the lesion in the region of the cortex of the parietal lobe, a tendency which was strengthened by the encephalogram, which suggested atrophy in that region of the brain. It having once been decided that the major disturbance was due to encephalopathy of arteriosclerotic origin, the symptoms involving the neck were explained as an incidental disturbance due to spondylitis. It may be mentioned here that many observers have pointed out that when roentgenograms show spondylitic or similar changes in the vertebrae it is unwise to conclude that these changes are the cause of the spinal symptoms.

In the second case, except for the general symptoms of an intracranial expanding lesion, the only localizing signs were the astereognosis and the associated slight sensory changes. These were considered as localizing signs of a tumor of the parietal lobe. However, since it is my contention that these signs may be the result not only of parietal lesions but of pressure on other parts of the brain, I believe that ventriculography would have furnished the only way of deciding on the location of the tumor before craniotomy.

In reviewing the errors in diagnosis in these 2 cases it must be remembered that it is much easier to see why the mistakes were made than to prevent the errors in the first place. Nevertheless, the erroneous impression of the lesions was not gained from overemphasis of certain misleading localizing signs, which is often the case, but from the topographic localization in a certain part of the brain of a sign which may have been due also to disturbances of other parts of the central nervous system. I contend that astereognosis does not necessarily indi-

cate a lesion of the parietal lobe but that it is often present as the result of a tumor protruding through the foramen magnum, with consequent pressure on the lower part of the medulla oblongata and the uppermost cervical portion of the spinal cord. That the astereognosis resulting from a tumor in the region of the foramen magnum shows the same sensory attributes as "pure" astereognosis resulting from a lesion in the parietal lobe is shown especially in case 2, in which there were no sensory or motor changes except astereognosis of the hand with slight changes in the sense of position and two point discrimination. Indeed, one finds occasional reports in the literature of the occurrence of isolated unilateral astereognosis as a result of lesions in parts of the nervous system other than the parietal lobe.

REVIEW OF THE LITERATURE

The first to draw attention to the fact that a tumor in "the posterior portion of the cerebellum" may cause astereognosis was probably Cushing. In 1923 he[8] reported a case in which he had preformed an exploratory cerebral craniotomy and had encountered nothing abnormal, but subsequently had observed a tumor in the posterior fossa. He stated:

> The other point of interest concerns Mr. E. H's astereognosis which made us suspect a parietal lobe lesion. . . . We . . . shall hereafter regard astereognosis as a symptom that may accompany a tumor in the posterior portion of the cerebellum, which can in some way involve the sensory pathway.

The patient was presented at a clinic held at a meeting of the American Neurological Association, at Boston, May 31, 1923, "from the standpoint of astereognosis produced by a cerebello-medullary lesion —a suggestion which was received with skepticism by members of the Society."

Subsequently, Kennedy,[9] in discussing this case, pointed out that astereognosis occurs in association not only with cortical or subcortical but also with peripheral, spinal and thalamic lesions. He stated that as a result even of purely cortical or subcortical postrolandic lesions there is in addition to astereognosis a quantitative reduction in kinesthetic sensibility and in the delicacy of response to the compass test.

Cushing and Bailey[10] cited 3 cases of cerebellar hemangioblastoma associated with unilateral astereognosis, in which the solid tumor itself

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8. Cushing, H.: Notes on a Series of Intracranial Tumors and Conditions Simulating Them, Arch. Neurol. & Psychiat. **10**:605 (Dec.) 1923.

9. Kennedy, F.: Astereognosis, Arch. Neurol. & Psychiat. **12**:305 (Sept.) 1924.

10. Cushing, H., and Bailey, P.: The Hemangioblastomas, in Tumors Arising from the Blood Vessels of the Brain, Springfield, Ill., Charles C. Thomas, Publisher, 1928, pt. 2, cases 16, 19 and 20.

or the cyst protruded through the foraminal ring. In commenting on the problem of astereognosis in association with tumors of that region, they wrote:

> The primary cerebral exploration doubtless might have been avoided by early resort to a ventriculogram; but had the exploration not been made, we might still be in doubt as to the possibility of a coexistent parietal lesion.

Roussy and Lévy [11] had a patient under observation whose prominent symptom was astereognosis of the right hand. An exploratory cerebral craniotomy was made for a tumor of the parietal lobe, but no tumor was seen. The patient continued to grow worse, and there soon developed astereognosis in the left hand without any other sensory changes; he died of sudden dyspnea and "cardiac collapse" two weeks after the craniotomy. Autopsy revealed a large infiltrating intramedullary glioma, which destroyed most of the medulla, reached to the inferior part of the pons and infiltrated and destroyed parts of the first cervical segments of the spinal cord. This experience led the authors to conclude that a tumor of the medulla may produce sensory dissociation suggestive of a lesion of the parietal cortex. Their main conclusions were essentially the same as mine.

Apparently, no other cases in which a similar error was due to the presence of astereognosis have been reported since. I have considered it important, therefore, to add the present 2 cases to the list of those reported.

Two other cases of tumor protruding through the foramen magnum with associated astereognosis are recorded in the literature; in these instances, however, the astereognosis was mentioned only as one of the findings, and no significance was attached to it.

Cushing [12] recorded the case of a man aged 34 with a cerebellar neoplasm of five years' duration who on admission had all the classic signs of a cerebellar tumor and astereognosis on the right side. At operation a median posterior cerebellar astrocytoma was observed, with a tonguelike projection into the spinal canal to the second cervical vertebra.

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11. Roussy, G., and Lévy, G.: Un cas de tumeur du bulbe à symptomatologie corticopariétale, in Contributions to Psychiatry, Neurology and Sociology, dedicated to the late Sir Frederick Walter Mott, New York, Paul B. Hoeber, Inc., 1929; Existence d'une dissociation, dite corticale, des troubles de la sensibilité par atteinte bulbo-protubérantielle et médullaire supérieure, Rev. neurol. **1**:145, 1930.

12. Cushing, H.: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C. Thomas, Publisher, 1932, pp. 180-181.

In the case reported by Bouttier and his associates,[13] a large intramedullary (?) glioma of the upper cervical portion of the cord extended through the foramen magnum into the medulla oblongata. The boy, aged 14, had astereognosis with only slight changes in the other forms of sensation. He also had weakness and atrophies in the hands, as well as in the rest of the upper extremities.

The accompanying table gives the essential data in the 8 cases recorded in which tumor in the region of the foramen was associated with astereognosis.

Batten [14] reported a similar case of a high cervical lesion associated with unilateral astereognosis and intact touch sensation. The lesion, however, was not verified.

On the other hand, many cases of varied types of tumor in the region of the foramen magnum have been reported in which no mention of astereognosis was made.[15]

Elsberg and Strauss,[16] in a report of the main clinical features in 6 cases of tumor protruding through the foramen magnum, did not mention astereognosis. They pointed out the comparative rarity of these tumors. In only 7 of 185 cases of tumor of the spinal cord did they see a new growth lying both in the uppermost part of the vertebral canal and in the posterior fossa.

Schott,[17] in discussing astereognosis in cases of cervical lesion, mentioned the tendency of some authors to differentiate between cortical astereognosis, or "stereoagnosis," which they ascribed to lack of perceptive, agnostic ability, and the noncortical astereognosis, or "stereoanesthesia," ascribed to lack of reception. Schott tabulated in cases

13. Bouttier, H.: Bertrand, I., and Mathieu, P.: Sur un cas de fibro-gliome médullo-bulbaire, Rev. neurol. **30**:763, 1923.

14. Batten, F. E.: Case of Astereognosis Probably Due to a Lesion of the Posterior Columns in the Cervical Region, Proc. Roy. Soc. Med. (Sect. Neurol.) **5**:150, 1911-1912, pt. 2.

15. Rhein, J. H. W.: Tumor in the Region of the Foramen Magnum, Arch. Neurol. & Psychiat. **11**:432 (April) 1924. Bailey, P.: A Study of Tumors Arising from Ependymal Cells, ibid. **11**:1 (Jan.) 1924. Abrahamson, I., and Grossman, M.: Tumors of the Upper Cervical Cord, J. Nerv. & Ment. Dis. **57**:342, 1923. Frazier, C. H., and Spiller, W. G.: An Analysis of Fourteen Consecutive Cases of Spinal Cord Tumor, Arch. Neurol. & Psychiat. **8**:455 (Nov.) 1922. Oldberg, E.: Surgical Considerations of Carcinomatous Metastases to the Brain, J. A. M. A. **101**:1458 (Nov. 4) 1933. Neuhof, H.: Giant Endothelioma of Medulla, S. Clin. North America **1**:1693, 1921.

16. Elsberg, C. A., and Strauss, I.: Tumors of the Spinal Cord Which Project into the Posterior Cranial Fossa, Arch. Neurol. & Psychiat. **21**:261 (Feb.) 1929.

17. Schott, E.: Ueber die Verwandbarkeit des Symptoms der Stereoagnosie in der topischen Diagnostik, Deutsche Ztschr. f. Nervenh. **80**:357, 1923-1924.

Clinical Data in Eight Cases of Astereognosis Associated with Tumor in the Region of the Foramen Magnum

No.	Author	Age, Years; Sex	Sensory and Reflex Changes	Papilledema	Internal Hydrocephalus	Suboccipital Headaches or Pain in the Posterior Cervical Region	Stiffness of Neck or Abnormally Fixed Attitude of Head	Exploration Negative for Tumor of Parietal Lobe	Type and Location of Tumor	Comment
1	Cushing and Bailey	24 M	Apparent astereognosis in left hand; slight impairment of muscle sense and slight sensory paresthesias on left side of body	Marked; bilateral	Marked internal hydrocephalus observed at autopsy	Present	Present	No operation; marked cerebellar signs	Hemangioblastoma, predominantly in posterior fossa	Died on same day after operation; tumor inseparable from floor of fourth ventricle
2	Cushing and Bailey	36 M	Total astereognosis in left hand; all deep reflexes markedly exaggerated on left	Bilateral	?	Present	None	No operation; marked cerebellar signs, although diagnosis doubtful	Hemangioblastoma, predominantly in posterior fossa	Patient doing well in 1928, although astereognosis persisted six years after operation
3	Cushing and Bailey	48 M	Complete astereognosis of left hand; loss of position sense in fingers and wrist of left hand, with questionable hypesthesia to all forms of sensation; exaggerated deep reflexes in both lower extremities	Early; bilateral	Slight internal hydrocephalus shown by ventriculogram	None	Present	Operation	Hemangioblastoma, predominantly in posterior fossa	Patient doing well in 1928, although astereognosis persisted five years after operation
4	Roussy and Lévy	55 F	Astereognosis of right hand; signs of slight right hemiparesis with impaired position sense and slight tactile hypesthesia in both right extremities; diminished vibratory sense in right upper extremity	None	?	Present	Present	Operation	Intramedullary glioma in upper cervical portion of spinal cord and in posterior fossa	Died in hospital
5	Rubinstein	58 M	Astereognosis and abarognosis in left hand; loss of position sense in fingers and toes on left; impairment of two point discrimination; diminution of vibration in left hand	None	None	Present	Present	Mistake in diagnosis, but no operation	Meningioma, predominantly in upper cervical portion of cord	Died in hospital
6	Rubinstein	29 M	Astereognosis of left hand; slight impairment of sense of position in fingers of left hand only; slight impairment of two point discrimination on whole left side (mostly in hand); vibration normal	Marked; bilateral with huge hemorrhages	Moderately marked internal hydrocephalus shown by ventriculogram	None	None	Operation	Hemangioblastoma of posterior fossa	Died after operation; tumor inseparable from floor of fourth ventricle
7	Cushing	34 M	Astereognosis on right (nothing said of other sensory findings or changes in motor power)	Present (?)	Present (?)	?	?	No operation	Astrocytoma of posterior fossa	Died a few days after operation, of ruptured acute duodenal ulcer
8	Bouttier, Bertrand and Mathieu	14 M	Astereognosis; very slight changes of all sensory modalities; weakness and atrophies in hands	Slight congestion of disks with slight dilatation of veins in fundi	?	?	?	No operation	Intramedullary glioma, mainly in upper cervical portion of spinal cord	Died; no operation

both of cortical and of noncortical disease all the sensory disturbances in the hand other than astereognosis and concluded that he was unable to differentiate between the two types of sensory loss.

In the presence of astereognosis, the following findings are helpful in placing the lesion in the region of the foramen magnum: prominence of a history of "rheumatic" pains about the neck and shoulders; stiffness of the neck, and a tendency to restrict the motion of the head or to keep it tilted to one side in a peculiar forced attitude. Sometimes there are variable loss of power in the four extremities, sensory loss below the neck and sphincteric disturbances. In many cases there are also signs of tumor in the posterior fossa, viz., headache, vomiting, papilledema, nystagmus and paresis of the ninth, tenth, eleventh and twelfth cranial nerves. These signs of an intracranial growth are also observed in cases of high cervical tumor and are due either to extension of the growth through the foramen magnum or to interference with circulation of the spinal fluid.[18]

Little, if any, experimental work has been done on astereognosis in animals. An attempt to study disturbances in barognosis due to cortical (parietal) lesions in primates has recently been made by Ruch and Fulton,[19] at Yale University. These experiments are being continued, and one may hope to have more exact information about the mechanisms involved in abarognosis and astereognosis.

SUMMARY AND CONCLUSIONS

Eight cases—2 of mine and 6 from the literature—of a tumor protruding through the foramen magnum with associated unilateral astereognosis are described. In 5 of the cases the astereognosis was in the foreground of the clinical picture.

It is shown that tumors in this region, whether extramedullary or intramedullary, give, by direct involvement or indirectly by pressure, sensory changes of the so-called cortical type, i. e., disturbances in stereognosis, position sense and two point discrimination without any concomitant changes in motor power or in the elementary sensations of touch, heat, cold and pain.

These sensory disturbances are probably due to a lesion in the medulla or the uppermost part of the cervical cord and are caused by pressure on, destruction of or interference with the vascular supply of the posterior columns and their nuclei, or the region of the decussation of the medial lemnisci when the lesion is higher in the medulla oblongata.

18. Elsberg, C. A.: Tumors of the Spinal Cord, Arch. Neurol. & Psychiat. **22**:949 (Nov.) 1929.

19. Ruch, T. C., and Fulton, J. F.: Cortical Localization of Somatic Sensibility, A. Research Nerv. & Ment. Dis., Proc. **15**:289, 1935.

These structures were the ones probably affected in most (6 of the 8) cases of extramedullary growth cited. In these 6 cases the tumor was situated on the posterior or the posterolateral surface of the medulla oblongata and of the upper cervical portion of the cord.

Tumors of this kind may be divided into two groups: (*a*) Spinal cord tumors growing in the vertebral canal and extending through the foramen magnum into the posterior part of the cranial chamber. In these cases symptoms of a tumor high in the cervical portion of the spinal cord are dominant. Spinal puncture may aggravate the condition and give rise to medullary symptoms, which should aid further in localizing such a tumor. The development of medullary signs after a spinal puncture should be considered as a reason for immediate surgical intervention to save life. (*b*) Intracranial tumors, essentially growths in the posterior fossa, extending through the foramen magnum into the vertebral canal. Here, the general symptoms of intracranial pressure are in the foreground, and the astereognosis is likely to be considered as due to a tumor of the parietal lobe. In these cases a ventriculogram showing symmetric internal hydrocephalus will be of great help in localizing the lesion.

* Dr. S. P. Goodhart, Chief of the Neurological Division, the Montefiore Hospital, New York, and Dr. Ernest Sachs, Chief of the Neuro-Surgical Division, the Barnes Hospital, St. Louis, permitted use of the clinical material, and Dr. Charles Davison, Neuropathologist to the Montefiore Hospital, allowed me to use some of the pathologic material.

Case Reports

THE LAURENCE-BIEDL SYNDROME OCCURRING IN A BROTHER AND SISTER

THOMAS K. RATHMELL, M.D., NORRISTOWN, PA., AND
M. A. BURNS, M.D., PHILADELPHIA

The Laurence-Biedl syndrome has been reported many times. Its cardinal characteristics of obesity, genital dystrophy, mental deficiency, retinitis pigmentosa and polydactylism are generally known. The etiology of the symptom complex is still a subject of controversy. Until this disputed point is settled, all variants or true syndromes of this type deserve recording.

Biedl [1] suggested that the syndrome is a familial form of dystrophia adiposogenitalis of cerebral rather than pituitary origin. This is generally accepted. Raab [2] expressed the belief that it results from dysfunction of the hypothalamic centers, caused by blocking off secretion from the pars intermedia by a high and massive dorsum sellae. It is generally agreed that a dorsum sellae of this type is not always present. The latest studies of Wislocki and King [3] disproved the theory of pituitary drainage into the hypothalamus. Ornsteen [4] explained the syndrome on the basis of a developmental defect of the ectopic zone of the prosencephalon, for the embryologic reason that the hypothalamus and the optic chiasm take origin from the ventral segment of the ectopic zone of Schulte and the end-brain from the cephalic segment. He ascribed polydactylism to the coupling of somatic genotypic defect characters with cerebral unit characters. Jenkins and Poncher [5] expressed the belief that of all the hypotheses advanced to explain the etiology of this syndrome that of Ornsteen is the most acceptable. They disagreed with the suggestion that the occurrence of polydactylism or other defects occasionally associated with this syndrome is a matter of chance coupling of somatic genotypic unit characters. They suggested

Read before the College of Physicians of Philadelphia, Dec. 28, 1936.

From the Laboratory of Pathology, the Norristown State Hospital; the Department of Neurology, the Jefferson Medical College Hospital and the Laboratory of Neuropathology, the Philadelphia General Hospital.

1. Biedl, A.: Deutsche med. Wchnschr. **48**:1630, 1922.

2. Raab, W.: Cerebral Obesity and Genital Atrophy, Wien. Arch. f. inn. Med. **7**:443, 1924.

3. Wislocki, J. B., and King, Lester S.: The Permeability of the Hypophysis and Hypothalamus to Vital Dyes, with a Study of the Hypophyseal Vascular Supply, Am. J. Anat. **58**:421 (March 15) 1936.

4. Ornsteen, A. K.: A Contribution to the Pathogenesis and Heredity of the Laurence-Biedl Syndrome (Dystrophia Adiposogenitalis, Retinitis Pigmentosa, Mental Deficiency and Polydactylism): Report of Three Cases in One Family, Am. J. M. Sc. **183**:256 (Feb.) 1932.

5. Jenkins, R. L., and Poncher, H. G.: Pathogenesis of Laurence-Biedl Syndrome, Am. J. Dis. Child. **50**:178 (July) 1935.

that a more probable explanation of the syndrome is one based on linkage of at least three genetic factors: one responsible for obesity and genital dystrophy, one for retinitis pigmentosa and one for polydactylism. They speculate as to whether the mental deficiency is due to one of these genes or is dependent on a linked gene.

In our opinion, when one knows few facts it is easy to formulate a hypothesis. We shall therefore accept the good features of all the hypotheses in the literature to date and refrain from introducing new theories. We present a report of two cases in a brother and sister admitted to the Norristown State Hospital. Certain features of the cases suggest strongly that they represent a variant of the syndrome.

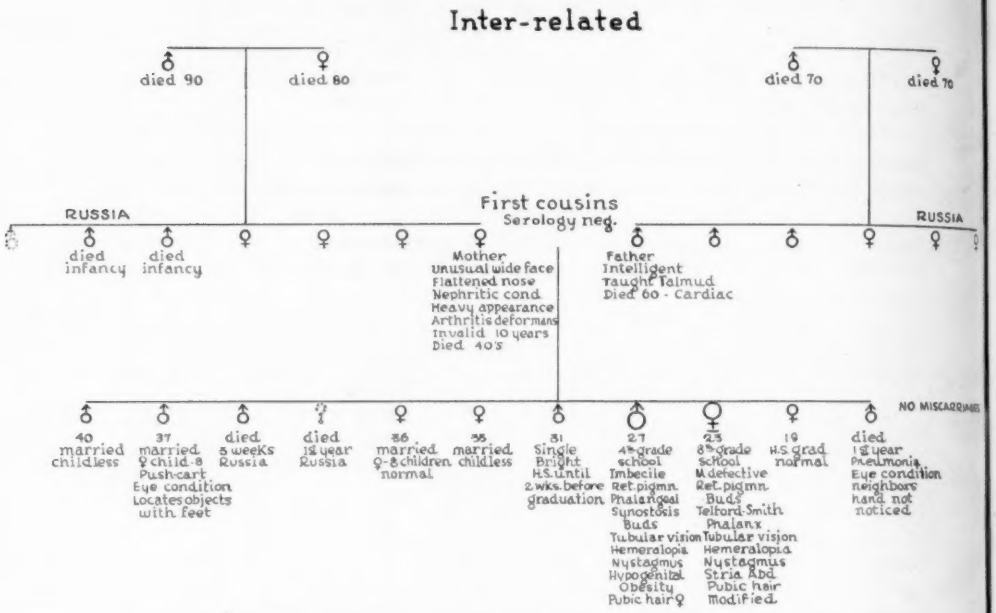

Fig. 1.—Genetic record of the family showing the Laurence-Biedl syndrome. Children 2 and 11 may be grouped with children 8 and 9.

REPORT OF CASES

Hereditary Factors.—The patients are the eighth and ninth of eleven children in a family of Russian Jews (orthodox). Both were born in Russia and came to America when young. Three children of the family died when under 1 year of age. There were no miscarriages. The first and sixth members of the family are childless, although both have been married a number of years. The second child presents signs which suggest that he probably conforms to the syndrome, but we were unable to locate him for examination. The eleventh child may also have been afflicted.

The parents were first cousins; their serologic reactions were normal. The father taught the Talmud and died at the age of 60, of cardiac failure. The mother was an invalid for the last ten years of her life and is said to have had an unusually wide face, with a flattened nose. She died in her fortieth year. The essential features of the family tree are summarized in figure 1. The grand-

parents were interrelated; the grandmothers may have been sisters or the grandfathers brothers or among the four grandparents there may have been a brother and sister who married unrelated mates (fig. 1).

Histories.—Case 1: N. M., the brother, is now 27 years of age. He attended school to the fourth grade. Both he and his sister were regarded by other children in their locality as "queer." On admission to the hospital, in the late spring of 1934, he was found to be mentally deficient—intelligence quotient, 42 (calculated on a 15 year basis)—and he was classified as an imbecile.

He is short, stocky and rather obese, and his appearance suggests endocrinopathy. Fat is abundant about the hips. His build is of the hypogenital type, with a few female secondary sex characteristics. There are a few pubic hairs. The thoracic interspaces are obliterated with adipose tissue. His eyesight is impaired, and there is marked to and fro lateral nystagmus (fig. 2).

Case 2: E. M., the sister, is now 23 years of age. She attended school to the eighth grade but always had trouble. She was mentally deficient—intelligence quotient, 64 (calculated on a 15 year basis)—and her case was classified as that of high grade mental deficiency.

She is well nourished, with a rather thick abdominal wall. Her eyesight is impaired, and she has lateral nystagmus. The distribution of pubic hair suggests the male pattern (fig. 3).

Further examination of the patients and more detailed study led to finding the additional features by which the syndrome is clinically recognizable. We report them graphically (table).

Eyegrounds.—The eyegrounds were studied by Dr. F. C. Parker,[6] of the staff of the Wills Hospital. He reported: "The boy's eyes showed a broad scleral ring with thinning of the retinal pigment. Choroidal circulation was seen over the entire eyeground. The vessels were threadlike; the nerves were pale and atrophic. There was a deposit of pigment of the 'bone corpuscle' type anteriorly and on the nasal side of the left eye. The girl's eyes showed threadlike vessels and atrophy of the optic nerve, with an isolated atrophic area above the disk of the left eye. On the nasal side of the left disk, well forward and in a location similar to that in the brother's eye, there was a deposit of pigment in the typical 'bone corpuscle' formation. The diagnosis is retinitis pigmentosa, with only tubular vision."

The patients both show obvious visual deficiency and, on questioning, admit that day vision is more satisfactory than night vision. We suspect that they also have hemeralopia, or night blindness. Their mental condition does not justify complete acceptance of their own evaluation of this sign.

Examination of the Genital Organs.—At no time during our observation of the brother have we been able to identify spermatozoa in the urine. The prostate was of normal consistency, but rather small; no secretion was obtainable after prostatic massage. We believe that this opinion is not prejudiced.

Pelvic examination of the sister showed apparently normal structural relationship of the external genitalia. The introitus was virginal; on rectal study the cervix was barely palpable and seemed to occupy a high intrapelvic position. There were no adnexal masses. The skin of the abdomen showed many white striae, which suggests sudden gain and loss of weight. From repeated questioning, we believe that the menstrual history has been relatively normal.

6. Parker, Frank C.: Personal communication to the authors.

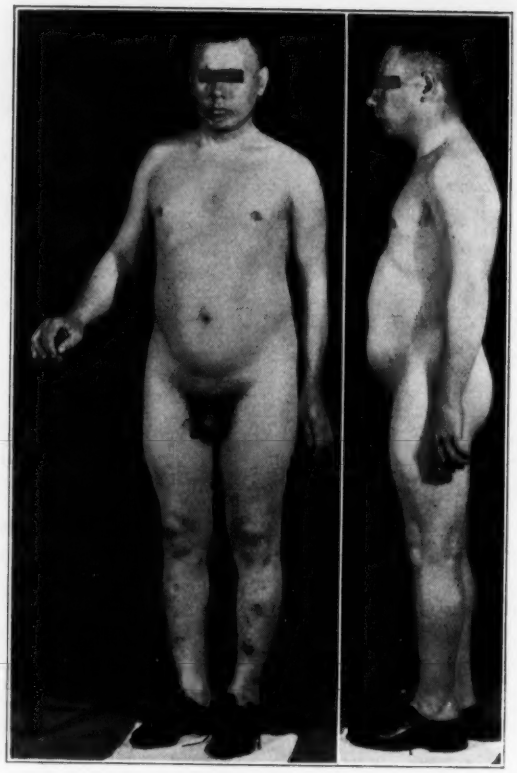

Fig. 2.—Frontal and lateral views of the brother.

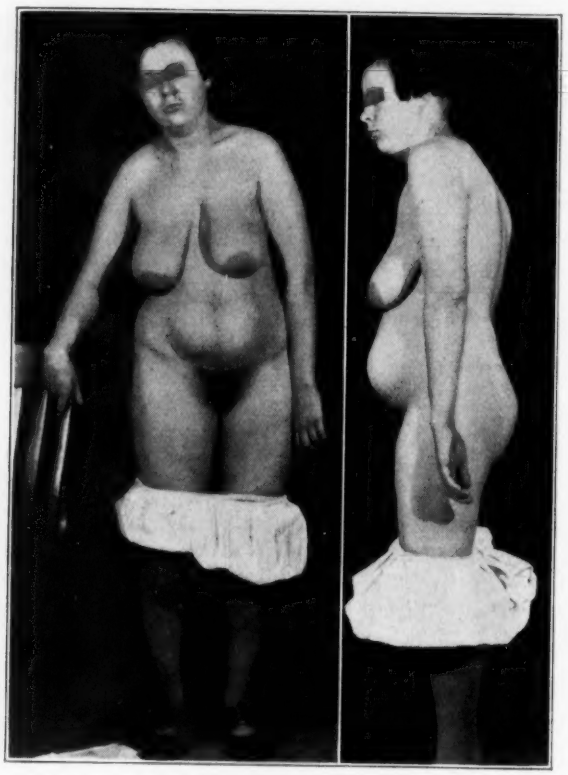

Fig. 3.—Frontal and lateral views of the sister.

Roentgenologic Studies.—The plates of the skulls in both cases are shown in figure 4. In the sister's skull there is some separation of both the frontoparietal and the occipitoparietal sutures, with greater increase in the convolutional markings than is usually seen in an adult of this age. There is thinning of the internal plate, particularly in the frontal region. The sphenoid sinus is much larger than

Clinical Findings in Two Cases of the Laurence-Biedl Syndrome

	Brother	Sister
Weight	153 lb.—61.2 Kg.	141 lb.—56 Kg.
Height	60 inches—165 cm.	61 inches—167.75 cm.
Blood pressure, mm.	120/90; 100/80	110/75; 110/90
Electrocardiogram	Normal	Vagotonic type
Basal metabolic rate	—6, —1	+22 (excited), —22, —28
Serologic reactions	Negative	Negative
Sugar tolerance		
Fasting	90.9 mg.	90.9 mg.
½ hour	174.2 mg.	124.8 mg.
1 hour	166.6 mg.	111.1 mg.
2 hours	124.8 mg.	95.2 mg.
3 hours	117.6 mg.	90.9 mg.
Blood chemistry		
Urea nitrogen	16.12 mg.	17.1 mg.
Phosphorus	4.7 mg.	4.6 mg.
Calcium	10.2 mg.	10.2 mg.
Phosphatase (Bodansky)	7.4 units	5.4 units

Mosenthal test	Volume, Cc.	Specific Gravity	Volume, Cc.	Specific Gravity
8 a. m.	305	1.003	180	1.038
10 a. m.	305	1.004	200	1.010
12 noon	305	1.003	295	1.008
2 p. m.	310	1.003	235	1.010
4 p. m.	302	1.004	265	1.008
6 p. m.	85	1.015		
Night	315	1.012	600	1.012
	1,927		1,775	

Friedman test	.....	No follicular hemorrhage
Urea clearance	Standard	Maximum
1 hour	58%	58%
2 hours	42%	106%

Blood count

	Hemoglobin, Gm.	Red Cells, Millions	White Cells, Thousands	Multiple Index	Schilling Index	Neutrophils: Myeloblasts	Neutrophils: Promyelocytes	Neutrophils: Myelocytes	Neutrophils: Metamyelocytes: Juvenile	Neutrophils: Metamyelocytes: Stab	Neutrophils: Segmented	Neutrophils: Total	Lymphocytes: Lymphoblasts	Lymphocytes: Large	Lymphocytes: Medium	Lymphocytes: Small	Lymphocytes: Total	Monocytes	Eosinophils	Basophils	Mature Neutrophils per Cu. Mm.
Normal	15.4	5.0	7.5	1	1-16	0	0	0	0	4-16	64	68	0	5	1	20	26	4	1	1	4,800
Boy	14	5.3	7.7	8	½	0	0	0	0	12	23	35	0	0	7	39	46	8	10	1	1,771
	The red cells were microcytic and hypochromic																				
Girl	12	4.9	8.0	5	½	0	0	0	0	15	43	58	0	3	4	25	32	6	3	1	3,440
	The red cells were normocytic and hypochromic Qualitative changes red cells																				

normal and well pneumatized, even into the posterior clinoid processes. The sella is widened in the anteroposterior diameter and measures 12 by 10 mm. The floor is somewhat sclerosed. There is slight calcification of the pineal body. The floor of the anterior fossa shows considerable sclerosis of the orbital plates.

The skull of the brother shows a large sella; the floor is deepened, measuring 15 mm. in the anteroposterior and 12 mm. in the vertical diameter; yet the processes and floor show no thinning. There is no suggestion of rarefaction or sclerosis. The sphenoid sinus is larger than normal and well pneumatized. Con-

volutional markings are not increased. The occipitoparietal suture shows suggestive widening. The pineal body is slightly calcified but normally situated. The bones are normal.

The hands are normal in both cases. The roentgenographic findings in these cases were reviewed by Dr. Herman Ostrum.[7] In the sister's feet (fig. 5) there

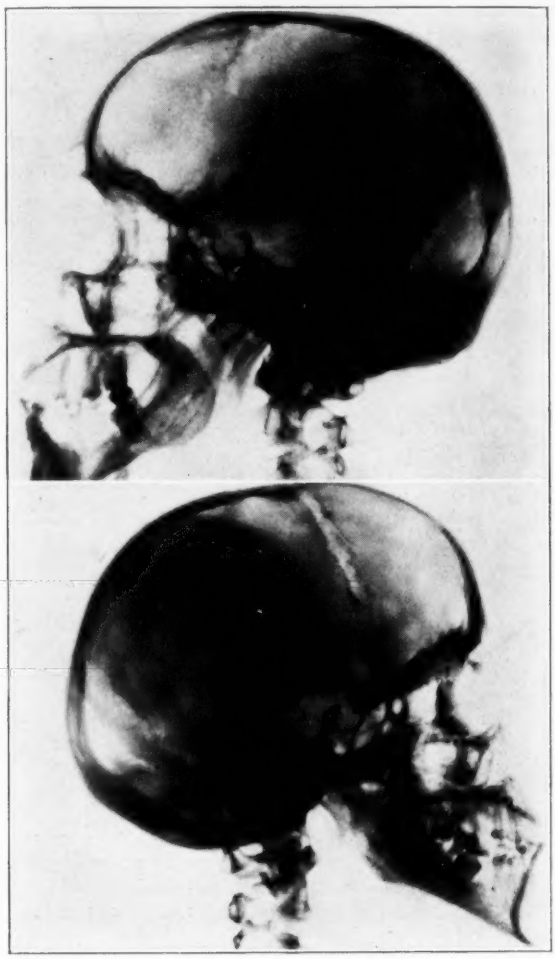

Fig. 4.—The upper roentgenogram shows the brother's skull with a large sella and widening of the occipitoparietal suture, and the lower, the sister's skull, with separation of both frontoparietal and occipitoparietal sutures and increased convolutional markings.

is symmetrical budding arising from the inner portion of the base of the terminal phalanx of both great toes, about 1 cm. from the joint space. The configuration

7. Ostrum, H.: Personal communication to the authors.

of the middle phalanges of both the fourth and the fifth toes suggests the Telford-Smith type, according to Clark.[8] Simian angulation of the first metatarsal bones is noticeable, with hypertrophy of the scaphoid bones.

The brother's feet (fig. 5) show phalangeal synostosis of the fourth and fifth toes bilaterally, with slight budding along their outer borders. The ungual tuber-

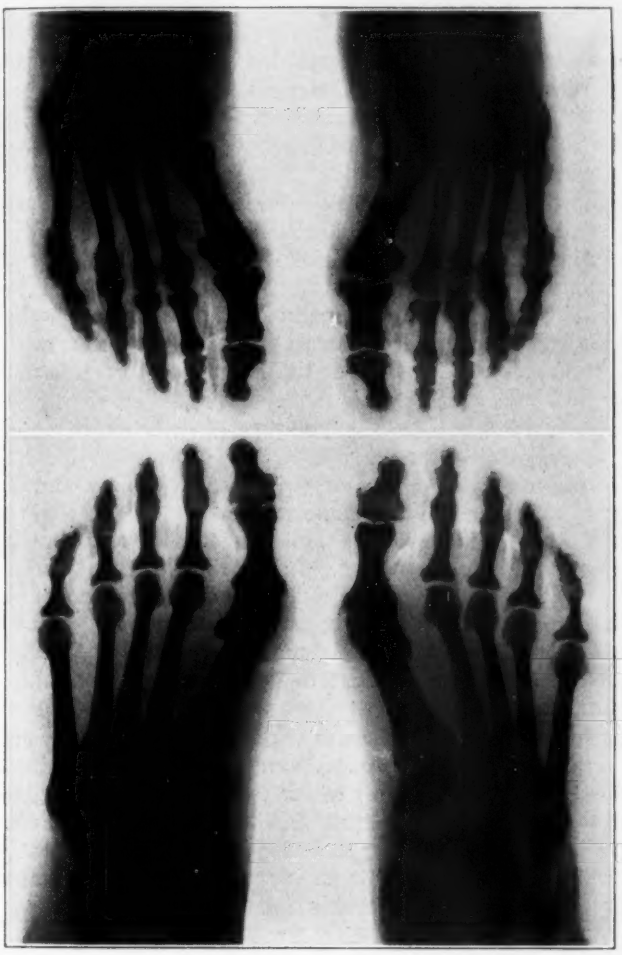

Fig. 5.—The upper roentgenogram shows the brother's feet, with phalangeal synostosis and budding, and the lower, the sister's feet, with symmetrical budding and phalanges of the Telford-Smith type.

osities in these toes are undeveloped. The middle phalanges of the second and third toes are shortened in the vertical and broadened in the transverse diameter.

8. Clark, D. M.: The Practical Value of Roentgenography of the Epiphyses in the Diagnosis of Pre-Adult Endocrine Disorders, Am. J. Roentgenol. **35**:752 (June) 1936.

Slight budding is noted along the inner portion of their bases. Angulation of the first metatarsal bones is not as marked as that in the sister's feet, and budding from the medial surfaces of the terminal phalanges of the first toes is less marked. In both cases the first phalanges are broadened, and in the brother the heads of the first metatarsal bones are broadened and flattened, but of smooth outline.

COMMENT

The association of obesity, genital hypoplasia or inadequacy, mental deficiency, retinitis pigmentosa, phalangeal synostosis in the brother and Telford-Smith phalanges in the sister, with budding in both cases, and the familial background led us to classify these cases as representative of the Laurence-Biedl syndrome.

A diagnosis of mental deficiency does not represent the true entity, from the standpoint of which one should approach the study of these patients. Since we are attempting to help them to adjust to a future noninstitutional environment, the true nature of the picture is important. The psychobiologic approach to study of the cases shows that mental deficiency is but one attribute of a well known syndrome, which, when discovered, enables one to plan for the future with greater understanding of the problem.

In a review of the findings in these cases, it is worthy of comment that the sister, while occupying a higher intellectual level than her brother, shows a greater degree of emotional instability and autonomic imbalance. Particularly is this demonstrated by reference to the results secured in the studies in her case. An electrocardiogram showed a slow, regular, vagotonic type of tracing. In the first basal metabolic test the rate was + 22; repetition of this study resulted in levels of — 22 and —28. The later determinations are more representative of the patient's true metabolic state. The original high level was due to her instability and emotional imbalance, incident to hospitalization and unfamiliarity with the procedure.

Curves for sugar tolerance were within normal limits in both cases. The data on the blood chemistry are not considered abnormal. We have no previous determinations with which to check the phosphatase levels. The results of the Mosenthal tests are not indicative of marked renal damage. The results of the urea clearance tests are not satisfactory, for we could not secure adequate cooperation from either patient. The values for the brother come within normal range, but those for the sister are variable. On one occasion she was given a liter of water, and we were still unable to secure a specimen. This appears to be additional evidence of autonomic imbalance. In her case we could not demonstrate any increase in concentration of the gonadotropic principle in the urine, as shown by the negative result of the Friedman test. Spinal puncture failed to show any increase in pressure of the cerebrospinal fluid in the sister.

Budding of the terminal phalanx of each great toe in these cases is not confused with exostosis. Exostoses are seen in from 4 to 5 per cent of persons, but not commonly at the age of these patients and certainly not in such bilaterally symmetrical positions.

Klenerman [9] reported cases of this syndrome in persons aged 40 and 72 years. In all probability, the syndrome in itself may not be expected to constitute a causative factor in early death.

Explanation of the clinical phenomena associated with involvement of the hypothalamus need not depend on embryonic defects within the cells of the hypothalamic area. In two cases of this syndrome studied in the laboratory of neuropathology at the Philadelphia General Hospital, congenital defects in the coats of the vessels supplying the hypothalamus (anterior choroidal [?] and posterior communicating arteries) have been observed.[10] These defects, while minor in themselves, may be the etiologic factor in establishing autonomic imbalance. Details of this mechanism are extraneous to our presentation and are therefore reserved for a later communication. Furthermore, the embryonic period of development of the medial coat of the cerebral vessels coincides with the formative period of the phalanges and retina (third and fourth months of fetal life).

SUMMARY

A brother and a sister from a Russian Jewish family are studied, and their mental deficiency is explained as but one attribute of the Laurence-Biedl syndrome.

The syndrome is based on the factors of familial history, mental deficiency, obesity, retinitis pigmentosa, hypoplasia or inadequacy of the genitalia with distribution of hair characteristic of the opposite sex, phalangeal synostosis, phalanges of the Telford-Smith type and budding of the phalanges.

Levels for the blood phosphatase are reported in this syndrome for the first time.

It is probable that two other members of this family were similarly affected.

DISCUSSION

DR. HELENA E. RIGGS, Philadelphia: In discussion of this presentation, I wish to make a preliminary report on a study of the brain in two cases of the Laurence-Biedl syndrome. To my knowledge, these are the first cases in which the brain has been studied histologically. I am able to disprove the hypothesis that there is a genetic defect in the prosencephalon to account for the clinical manifestation. Rather, I have seen evidence in the cerebral cortex and brain stem that there was widespread arrest in development in early intra-uterine life. My studies suggest that malformation of the visual cortex may play as large a role in the defective vision as the retinitis pigmentosa. The evidence of autonomic imbalance in cases of the Laurence-Biedl syndrome is not the result of embryonic defects in development of the hypothalamus. Rather, it is an abiotrophy, a progressive loss of function of the cells of the cerebral vegetative centers as a result of inadequate vascular supply. In both my cases it was possible to demonstrate defective development of the medial coat in the vessels supplying the region of the hypothalamus.

DR. M. A. BURNS, Philadelphia: Although the patients in the cases presented are children of blood relatives, we do not wish to give the impression that the Laurence-Biedl syndrome is the result of consanguinity. It is known that when

9. Klenerman, P.: Laurence-Moon-Biedl Syndrome: Report of Two Cases, J. Neurol. & Psychopath. **15**:329 (April) 1935.

10. Riggs, H. E.: Personal communication to the authors.

the stock is good, the progeny from intermarriage of relatives will not show mental defects, but when the stock is poor, any mental deterioration may be exaggerated in the offspring of such unions.

In cases of the Laurence-Biedl syndrome in which mental deficiency has played an important part, the patients have been segregated as mentally deficient in hospitals for mental disease, and further education has not been attempted. In the two cases reported here, one patient reached the eighth grade in school; the other attained the fourth grade. It is possible that they did not progress further because of lack of vision due to retinitis pigmentosa. If patients of this type could be educated much as are the blind, viz., by means of the Braille system, I believe that many who are now considered mentally defective could be educated, certainly to a degree at which they could take care of themselves. It is well known that many morons apparently do well in the community. Why, therefore, commit to the role of mental deficiency, or even to that of a low grade moron, patients who may be able to care for themselves outside an institution if their education is properly handled?

SOMATOTOPIC LOCALIZATION IN THE EXTRAPYRAMIDAL SYSTEM

S. Philip Goodhart, M.D., and Ben H. Balser, M.D., New York

In the course of the study of extrapyramidal diseases and their associated movements, an opportunity presented itself for the observation of 2 patients, twins, with hepatolenticular degeneration over a period of three years. During the early part of the period of observation, the beginning of the characteristic *Flügelschlagen* movements was observed in 1 twin. With the anticipation of progression of these movements, moving picture studies were made throughout the period.

REPORT OF A CASE

History.—In September 1934 Bertha and Ethel H., twin sisters, 16 years of age, were admitted to the neurologic service of the Montefiore Hospital. They were American-born Jewish girls of Austrian descent, their parents being first cousins; they had 2 brothers, aged 25 and 14, who were well. The family history was without significance for nervous ailments. In 1928 Bertha, at the age of 10, had a period of daily vomiting lasting about three months. Laparotomy was performed at another hospital, and cirrhosis of the liver was observed. She was well thereafter up to the age of 13, when her speech began to be slow and thick. At about the same time she realized that she was becoming sluggish mentally. Six months before admission she began to have persistent headaches.

Ethel's difficulties began when she was 15, at which time she noted difficulty in the use of her fingers in performing fine acts, such as opening her purse or powdering her face.

Examination.—Bertha, at the time of admission, was well developed and well nourished, with dull, expressionless facies; she was emotionally subdued, and her affective responses were somewhat fixed. Her gait was stiff and somewhat inelastic, and she was unable properly to perform rapid alternating movements. There were a generalized increase in muscular tonus, most marked in the right upper extremity, and slight generalized paresis, which became greater with exertion. There were automatic up and down movements of the tongue as it lay in the mouth. Associated movements in the right upper extremity were absent on walking. The deep reflexes were all increased, but there were no pathologic reflexes. Dysarthria was present. Kayser-Fleischer rings were present in both eyes.

At the same time, examination showed that Ethel was more alert; she was well developed and well nourished and tended somewhat toward facetiousness. The findings were much the same as those for her sister, with the additional fact that there was slight tremor of the right forefinger. This tremor had the characteristics of the so-called *Flügelschlagen* movements which have been described in cases of progressive hepatolenticular degeneration.

From the Neurological Division, the Montefiore Hospital.

Read at the Sixty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1937.

Diagnosis in both cases was progressive hepatolenticular degeneration. After the girls had been in the hospital two months it was noted that Ethel was beginning to have a similar tremor in the left forefinger, at which time moving pictures were taken to record these movements. Encephalograms made at that time showed dilatation of the anterior third of the lateral ventricles.

Course.—The patients were observed for the next two years. By January 1937 it was noted that the initial tremor in Ethel's right forefinger had now progressed to the point at which *Flügelschlagen* movements involved both hands and all the fingers. At this time Bertha had no movements of this nature in any

Figure 1

Figure 2

Fig. 1 (Ethel H.).—Print from a strip of moving picture film showing *Flügelschlagen* movements of both hands.

Fig. 2 (Bertha H.).—Print from a strip of moving picture film showing no movements of the hands or fingers.

of her fingers or in either hand, but there was some involvement of the right arm. Moving pictures of both patients were again taken. Figure 1 is a print of the moving pictures taken of Ethel at this time, showing the movements present in both hands. (This may be compared with figure 2, taken of Bertha, which shows no movements in the hands.)

The progressive localized involvement of finger after finger and then of the hands with movements of distinctly extrapyramidal type permits the conclusion that there is somatotopic localization in this system. The fact that in one of the sisters the arm rather than the fingers and hands is involved refutes any assumption that the fingers are involved first because they are more highly developed anatomic portions in man. Mingazzini,[1] in 1912, was perhaps the first proponent of such a theory of localization, but, like the Vogts,[2] he lacked sufficient evidence to substantiate his assumption. Cassirer [3] attempted to correlate spasmodic torticollis with a lesion localized in the anterior part of the caudate nucleus, but the observation of lesions elsewhere in the neostriatum weakens his argument.

It is interesting that a specific movement so curiously repetitious and of such gross amplitude should exhibit itself as a release phenomenon with destruction of parts of the extrapyramidal system. At least six types of spontaneous and involuntary movements are produced by removal of the inhibitory effects of the extrapyramidal system; namely, choreiform, athetoid, dystonic, parkinsonian, *Flügelschlagen* and hemiballistic movements. Three possible combinations may explain such localization of influence: first, segmental localization in both the basal ganglia and the corresponding area in the red nucleus, the common station through which extrapyramidal impulses must pass; second, segmentation in the basal ganglia and not in the red nucleus, and third, segmental localization in the red nucleus alone. In any case, the conclusion is that with the evidence presented it is justifiable to assume that there is somatotopic localization in the extrapyramidal system.

DISCUSSION

Dr. Charles Davison, New York: Clinically, Drs. Goodhart and Balser have convinced me of the possibility of somatotopic localization in the basal ganglia. It may be assumed that the dentate mechanism may also have something to do with this form of extrapyramidal symptom complex and that this structure may have a segmental arrangement. Unfortunately, the extrapyramidal syndrome in patients with this disease is so completely degenerated before autopsy that one is not able to correlate the finer movements that occurred earlier in the course of the disease with the pathologic changes distributed throughout the basal ganglia.

As stated by Dr. Balser, Cassirer, although he had a case of spasmodic torticollis, i. e., dystonia limited to the muscles of the neck and face, was unable to demonstrate segmental involvement of the striatum. The lesions in this instance were diffuse. More recently, Dr. Bernard Alpers, who studied a case of spasmodic torticollis, was unable to localize the dystonic phenomena of the muscles of the neck in any particular region of the basal ganglia. Histopathologically, therefore, there is no proof for segmental localization in the basal ganglia. This somatotopic

1. Mingazzini, G.: Das Linsenkernsyndrom, Ztschr. f. d. ges. Neurol. u. Psychiat. **8**:85, 1912.

2. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen der striären Systems, Leipzig, J. A. Barth, 1920 (Thomalla's cases, pp. 765-776; Westphal's case, pp. 776-781).

3. Cassirer, R.: Halsmuskelkrampf und Torsionsspasms, Klin. Wchnschr. **1**:53, 1922; Centralbl. f. d. ges. Neurol. u. Psychiat. **28**:513, 1922.

localization, which probably exists, can be demonstrated clinically, and in the future neurophysiologic experimentation may solve the problem. Slight proof for segmentation of the dentate nuclei was apparent to me in the study of the brain of a child who before death had presented choreoathetoid movements. The dentate nuclei in this case consisted of several segments instead of the usual convoluted sac. Segmentation probably exists early in life, and careful studies will probably demonstrate it.

Dr. Emanuel D. Friedman, New York: Drs. Goodhart and Balser have called attention to clinical facts which all have noted for some time. Every one with any experience has recognized the segmental forms of dystonia—dystonia of the muscles of the neck and the pelvic musculature, dystonia in the form of dysgraphia (described by my colleague, Dr. Samuel Brock) and the striate, or dystonic, foot. There is no doubt in my mind as to the clinical frequency of these focal dystonias. They are really fragments of decerebrate rigidity.

My colleagues and I had a dramatic illustration of focalized dystonia in a case at the Bellevue Hospital. The man had acquired syphilis, and years later segmental and focal dystonia developed in the tongue. Every time that he started to speak his tongue curled up in his mouth, making articulation difficult. Even in the absence of definite pathologic evidence of these lesions, it is worth while recording these clinical instances of isolated forms of disease of the basal ganglia. They certainly point to segmentation and somatotopic localization in the extrapyramidal system.

SPECIAL ARTICLES

PATHOGENESIS OF ENCEPHALITIS OCCURRING WITH VACCINATION, VARIOLA AND MEASLES

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The anatomic changes in encephalitis associated with vaccination, variola and measles are so similar as to suggest a common pathogenetic factor. This is further indicated by the fact that this type of encephalitis occurs in a group of clinical entities all characterized by an exanthema. Spielmeyer [1] has pointed out the errors one is led into by drawing conclusions as to pathogenesis from anatomic observations alone. Other biologic sciences should be called on to help in the solution of this problem. I wish, therefore, to refer to some past studies on the immunology of the exanthema and to correlate them with those on the associated encephalitis.

Since more is known concerning the local and general tissue reaction to the vaccine virus than of that to the viruses of smallpox and measles, knowledge of the pathogenesis of the vaccine virus will give a clearer insight into that of the encephalitis associated with the exanthema. Pirquet,[2] in his studies on vaccination and allergy,[3] demonstrated that the cutaneous lesion of vaccination passes through a sequence of changes which are remarkably constant. He divided the primary lesion of vaccination into two parts: (1) the papule, which develops at the site of inoculation and which he showed to be the nonspecific reaction to the

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1. Spielmeyer, W.: Infektion und Nervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:161, 1930.

2. von Pirquet, C.: Klinische Studien über Vakzination und vakzinale Allergie, Leipzig, Franz Deuticke, 1907.

3. The term "allergy" is used throughout this paper as the specific biochemical reaction produced in the body from invasion of a foreign agent which leads to specific immunity or hypersensitivity of the body to the foreign agent. It is recognized that immunity and hypersensitivity may be separate biologic phenomena. This definition purposely avoids a definite statement as to whether the specific biochemical reaction occurs in the blood plasma, the fluid of the tissue spaces or between one of these and the blood or tissue cells. The cellular changes seen microscopically are considered secondary to the antigen-antibody reaction.

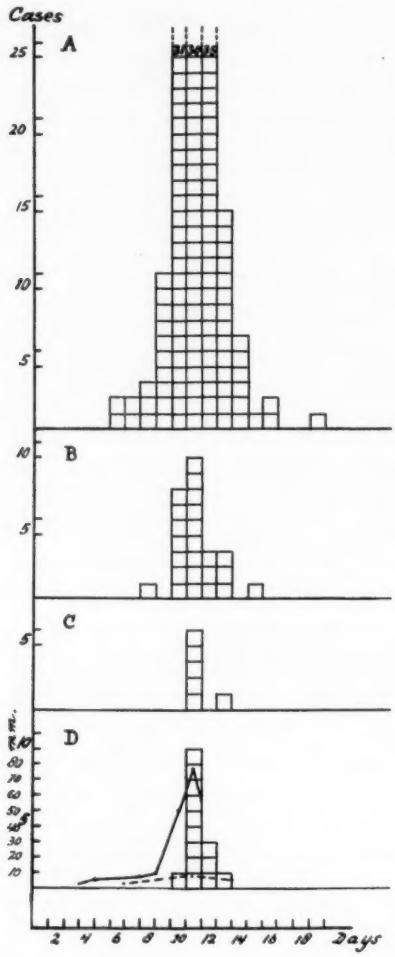

Chart 1.—Chart showing the relationship between the incubation periods of vaccinal encephalitis and the general and local vaccinal eruptions and the acme of the reaction in the vaccination wound. *A* represents the incubation period in one hundred and thirty-seven cases of vaccinal encephalitis (Bastiaanse), with an average period of eleven days; *B*, the incubation period in twenty-four cases of local vaccinal exanthema (Pirquet), with a mean period of eleven days; *C*, the incubation period of the general vaccinal eruption in six cases with a mean incubation period of eleven days, and *D*, the day on which the acme of the reaction was reached in the vaccination wound, calculated from the time of inoculation in fourteen cases (Pirquet). Again, it will be noted, this usually occurs on the eleventh day. The continuous line represents the growth in diameter of the areola, expressed in millimeters, on successive days, and, similarly, the dotted line represents that of the papule (Pirquet). The ordinates represent the number of cases, and in *D*, also the diameter of the areola and papule, expressed in millimeters. The abscissas represent the time expressed in days.

virus, and (2) the areola, an area of hyperemia which develops about the papule, appearing about the fourth day after vaccination, and is the specific reaction to the virus. Its diameter increases slowly until the eighth day, when it rapidly increases, reaching a maximum at the same time that the papule attains its acme, on the eleventh or twelfth day (chart 1 *D*). Antibodies appear in the body at least by the fifth day,[4] and a specific precipitin reaction can be demonstrated in man by the eighth day. Also, the virus is known to reach the blood stream a few days after vaccination and has frequently been demonstrated in the body of man and animals, on from the fourth to the twelfth day. Pirquet expressed the belief that the areola, which develops about the time, or a little before, antibodies can be demonstrated, results from the reaction of antibodies in the surrounding tissues and the virus in the papule. He pointed out that the increase in the diameter of the areola follows a curve which simulates the curve for production of antibodies from injection of horse serum, as proved by daily precipitin tests. On the eighth day, with the sudden increase in production of antibodies, the areola begins to grow rapidly, until the antigen in the live tissues of the papule is overcome (i. e., between the tenth and the twelfth day), when healing begins. That this antigen-antibody reaction is occurring in other parts of the body is evident from the rise in temperature, which is first noticed shortly after the appearance of the areola. The temperature further increases suddenly on the eighth day, with the sudden increase in diameter of the areola. However, that the fever is not due alone to the reaction at the site of inoculation is known from the fact that fever persists even after excision of the vaccination wound and also from the fact that the antigen and antibodies exist throughout the body. Histologically, this allergic state is usually demonstrable only in the vaccination wound. From experiments with vaccination of animals it is known that changes of a histopathologic nature may also occur in other organs of the body.[4]

Two cutaneous reactions that sometimes occur with vaccination help to link it with the encephalitis: (1) the local vaccinal exanthema developing about the site of inoculation (the most frequent) and (2) the general vaccinal eruption (the less frequent). Chart 1 shows the relation of the appearance of the local (*B*) and the general (*C*) exanthema to the course of the primary lesion (*D*). The development of the local and the general exanthema coincides with the acme of the local vaccinal lesion. In all cases of vaccinal eruption (local or general) which Pirquet observed, the eruption always occurred a few hours before or at the time of the acme of the reaction in the vaccination wound. One may conclude from his work that the incubation period of the local and

4. Kolle, W.; Kraus, R., and Uhlenhuth, P.: Handbuch der pathogenen Mikroorganismen, ed. 3, Jena, Gustav Fischer, 1930, vol. 8, p. 2.

the general eruption following vaccination corresponds to the height of the specific reaction of the body to the invading etiologic agent, which is thought to be an interplay between antibody and antigen.

What relation does vaccinal encephalitis have to the aforementioned points? The consistency of the incubation period of exanthema encephalitis has been referred to in the literature.[5] Van Bogaert[6] pointed out the relationship between the onset of the encephalitis and the stage of development of the primary vaccination wound. Chart 1 *A* shows the incubation period in one hundred and thirty-seven cases of vaccinal encephalitis reported by Bastiaanse.[7]

In 90 per cent of the cases there was an incubation period of from ten to twelve days, which coincides closely with the incubation periods of the local and the general exanthema of vaccination. As is true of the local and the general eruption, the onset of cerebral symptoms occurs at the time when the tissue reaction at the site of the local wound and throughout the body is at its height. Comby[8] reported two cases of vaccinal encephalitis, in one of which the onset was six days and in the other eight days after revaccination. Querido[9] reported a case of vaccinal encephalitis in which the onset was five days after revaccination. The anatomic observations were characteristic of vaccinal encephalitis. These short incubation periods could reasonably be due to an accelerated cerebral reaction to the vaccine virus, similar to the accelerated local reaction at the site of inoculation following revaccination. These points suggest that the biologic forces responsible for the vaccination wound and the local and general vaccinal exanthemas are also responsible for the cerebral involvement. When one adds to this the evidence showing that the cerebral tissue as well as other organs of the body are immune to the virus after vaccination, one has more than suggestive evidence. Bijl and Frenkel[10] showed that rabbits previously vaccinated remain well after intracerebral inoculation of the vaccine virus, while unvaccinated animals die a few days after cerebral injection. Also, the cere-

5. Glanzmann, E.: Die nervösen Komplikationen der Varizellen, Variola und Vakzine, Schweiz. med. Wchnschr. **57**:145 (Feb. 12) 1927. Kolle, Kraus and Uhlenhuth.[4]

6. Van Bogaert, Ludo: Les manifestations nerveuses au cours des maladies éruptives, Rev. neurol. **1**:150, 1933.

7. van Bouwdijk Bastiaanse, F. S.: Die in Holland beobachteten Fälle von Encephalomyelitis post-vaccinalis bis zum 1. Januar 1929, Ztschr. f. d. ges. Neurol. u. Psychiat. **134**:657, 1931.

8. Comby, M.-T.: Les encéphalites aiguës post-infectieuses de l'enfance, Paris, Masson & Cie, 1935.

9. Querido, A.: Encephalitis nach Wiederimpfung mit fehlender örtlichen Reaktion nebst einigen Bemerkungen ueber die Histopathologie der Encephalitis post vaccinationem, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:423, 1930.

10. Bijl, J. P., and Frenkel, H. S.: Experimentelle Untersuchungen über Encephalitis postvaccinatoria, Zentralbl. f. Bakt. (Abt. 1) **112**:412 (June 28) 1929.

bral tissue of vaccinated rabbits when incubated with the vaccine virus is capable of making the virus inactive, while brain tissue of nonvaccinated rabbits when incubated with the virus does not inactivate it. These authors also inactivated the vaccinia virus by incubating it with cerebral tissue from a child who had died of vaccinal encephalitis. As the skin acquires immunity to further inoculations from the primary vaccination (i. e., for a few years) so the cerebral tissue becomes immune to the vaccine virus. Therefore, it is probable that the specific allergic state of the body resulting from vaccination influences the central nervous system as well as the skin and other organs of the body. One may mention other conditions in which an allergic state of the nervous system exists. The immunity of the brain to a second attack of poliomyelitis was demonstrated by Flexner and his co-workers. The hypersensitive state of the brain to intracerebral injections of horse serum in animals which had previously been sensitized was demonstrated by Davidoff, Seegal and Seegal.[11] Radiculitis following injections of antitetanus serum was reported by Ayer.[12] The allergic reaction to tuberculin of the meninges of tuberculous guinea pigs was produced experimentally by Burn and Finley.[13]

The anatomic changes present in these conditions differ from those seen in the type of encephalitis under discussion and also from one condition to another. The reaction produced in the experiment of Davidoff, Seegal and Seegal was a local hemorrhagic and polymorphonuclear response, plus a glial reaction and widespread edema. The meningeal reaction to tuberculin in the studies of Burn and Finley was a polymorphonuclear response. This variety of tissue response to antibody-antigen reaction in the central nervous system coincides with that of similar cellular responses to antibody-antigen reaction known to occur in other parts of the body. Davidoff and the Seegals, in fact, described their changes as an Arthus phenomenon of the brain. The factors responsible for the different cellular responses to allergic reaction are not within the scope of this paper to discuss.

Because of the close similarity, from both the immunologic and the clinical standpoint, of the virus of smallpox to that of vaccinia, there is little reason to doubt that the etiologic and pathogenetic factors of encephalitis in the former are the same as those in the latter. In smallpox the sequence of events, including the incubation period, the production of antibodies, which reaches a climax in the exanthema, and the resulting immunity correspond to the pathogenesis of vaccination.

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11. Davidoff, L. H.; Seegal, B. C., and Seegal, D.: The Arthus Phenomena: Local Anaphylactic Inflammation in Rabbit Brain, J. Exper. Med. **55**:163, 1932.

12. Ayer, J. B.: Radiculitis Following Injections of Antitetanic Serum, J. Nerv. & Ment. Dis. **81**:676, 1935.

13. Burn, C. G., and Finley, K. H.: The Rôle of Hypersensitivity in the Production of Experimental Meningitis, J. Exper. Med. **56**:203, 1932.

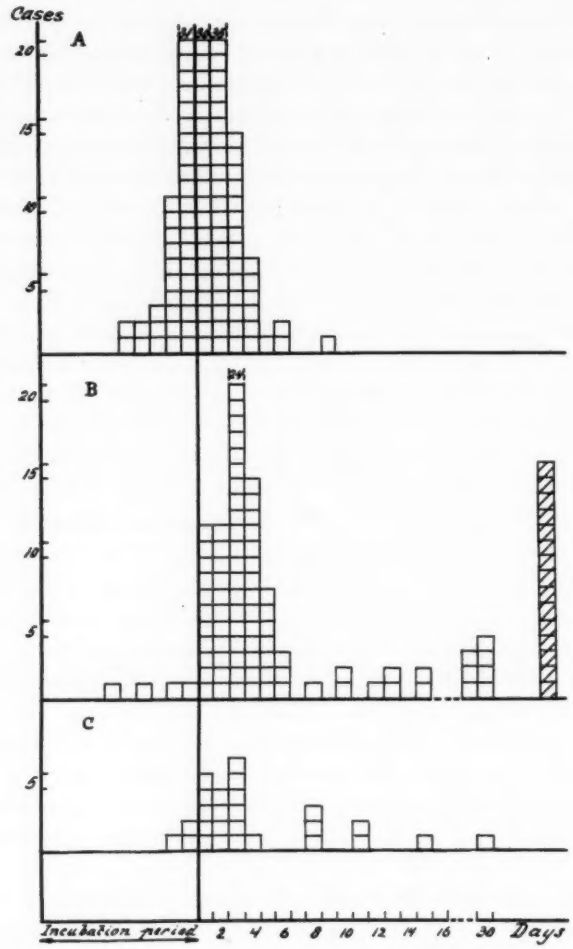

Chart 2.—Incubation periods in cases of encephalitis following vaccination, measles and variola. The heavy vertical line represents the onset of the exanthema. As exanthema does not occur in vaccinal encephalitis, the relationship of the vaccinal eruption to the encephalitis was supplied from chart 1. *A*, the graph for one hundred and thirty-seven cases of vaccinal encephalitis (Bastiaanse); *B*, that for one hundred and nine cases of measles encephalitis (Ford, F. R.: The Nervous Complications of Measles, *Bull. Johns Hopkins Hosp.* **43**:140, 1928) and *C*, that for twenty-six cases of variola encephalitis (Turnbull, H. M., and McIntosh, J.: Encephalomyelitis Following Vaccination, *Brit. J. Exper. Path.* **7**:181, 1926), show the onset of cerebral symptoms with relation to that of the cutaneous eruption in case of each exanthema. In *B* the column on the right shows fifteen cases in which the onset of cerebral symptoms was reported as occurring during the convalescent period and which therefore could not be given a definite place in the chart. The ordinates represent the number of cases, and the abscissas, the number of days.

From chart *2 C* it is seen that the incubation period of variola encephalitis has approximately the same time relationship to the onset of the exanthema as vaccinal encephalitis to vaccinal exanthema.

Similarities exist between the pathogenesis of measles and that of vaccination. Not only is there a similar incubation period but, from the work of Blake and Trask [14] on experimental measles in monkeys, it is known that the virus may exist in the blood stream during the later part of the incubation period. Through the immunity conferred on the body by an attack of measles, it is known that antibodies must be an important factor in the pathogenesis of the lesions. The authors also suggested that immunity may be conferred on all tissues. Chart *2 B* shows the consistency of the incubation period in cases of measles encephalitis and its similarity to that of encephalitis following vaccination and smallpox and to the eruption of measles.[15]

The type of encephalitis under discussion occurs in infectious diseases other than those described here. Scheidegger [16] studied the brains in three cases in which the fatal illness began as an infection of the upper respiratory tract and signs of encephalitis developed from about ten days to two weeks later. The pathologic picture in the brains in these cases could not be distinguished from that of encephalitis following vaccination, variola and measles. Varicella encephalitis probably also belongs to this group. To my knowledge, only one such case has been thoroughly studied from the pathologic standpoint, that studied by Zimmerman and Yannet.[17] An allergic factor in these conditions, therefore, cannot be disregarded. Putnam [18] emphasized the similarity of lesions in some cases of multiple sclerosis to those of the infectious encephalitides.

In the preceding discussion on the pathogenesis of this group of encephalitides, evidence has been given to support the belief that they are

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14. Blake, F. G., and Trask, J. D.: Studies on Measles, J. Exper. Med. **33**: 413, 1921.

15. In encephalitis following measles and smallpox the onset of symptoms occurs from two to four days after the exanthema, while in that following vaccination the onset of symptoms comes at the end of, or shortly after, the known incubation period of the vaccinal exanthema. The incubation period of encephalitis following measles and smallpox is therefore a day or two longer than that of vaccinal encephalitis. The first forms are associated with an exanthema, while vaccinal encephalitis is not. That the presence of the exanthema prolongs the incubation period of the encephalitis is given as a suggestion.

16. Scheidegger: Personal communication from the author.

17. Zimmermann, H. M., and Yannet, H.: Nonsupportive Encephalomyelitis Accompanying Chickenpox, Arch. Neurol. & Psychiat. **26**:322 (Aug.) 1931.

18. Putnam, T. J.: Studies in Multiple Sclerosis: VII. Similarities Between Some Forms of "Encephalomyelitis" and Multiple Sclerosis, Arch. Neurol. & Psychiat. **35**:1289 (June) 1936.

the result of a response of the central nervous system to the virus of the exanthema. Evidence has been offered indicating that the response of the brain is allergic, as in other tissues or organs of the body, and that the incubation period of the encephalitis corresponds to that of the particular exanthema with which it occurs. True, the evidence is indirect, and certain points are not clear or consistent. For instance, why does one not more often see complications of the central nervous system following this group of exanthemas? It can be pointed out that an eruption seldom follows vaccination; yet when it does occur, one does not question the direct relationship of the eruption to the vaccination. Poliomyelitis is not always followed by complications of the central nervous system, and only a small minority of persons with immunity to the virus of poliomyelitis have had the clinical disease. Therefore, that encephalitis does not always follow vaccination or an exanthema is in itself no reason for doubting that the etiologic agent and pathogenetic factors in these processes could also be the cause of the encephalitis. Another stumbling-block is that not in all cases of encephalitis does the disease occur at the time of the eruption. Some of the cases in which encephalitis develops late could probably be explained if one could observe the onset of the pathologic process in the brain as one does in the skin. Observation of the onset of the encephalitis is dependent on that of neurologic symptoms and signs, which may not be noted early when the pathologic process in the brain appears. On the other hand, neurologic symptoms may be confused with prodromal symptoms, and thus the onset of encephalitis may be placed before that of the rash. Also to be remembered is that as yet little is understood of the reactions of hypersensitivity and immunity in the brain.

SUMMARY

Allergy (as defined in this article) is discussed as an important factor in the pathogenesis of encephalitis associated with vaccination. variola and measles.

ROLE OF VITAMIN C IN METABOLISM OF NERVE TISSUE

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AND

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The problem of nervous and mental diseases related to deficiences of specific food factors has recently been reviewed by one of us.[1] It is now well established that vitamins A and B play an important role in the functioning of nerve tissue. Concerning the role of vitamin C in nervous economy little is known. It is our purpose in this paper to present, in addition to the results of our own studies, the recent data in this field, in an endeavor to understand the role of vitamin C in the metabolism of nerve tissue.

CHEMICAL STUDIES

Vitamin C is present in both the blood [2] and the cerebrospinal fluid [3] and is capable of passing from one to the other.[4] It is present in the brain and spinal fluid only in its reduced form,[5] whereas in the blood a portion of it occurs in the reversibly oxidizable form.[6] The subject of the vitamin C content of the blood, together with the urinary excretion of the vitamin, has been excellently reviewed in a series of papers by Wright and his associates.[7]

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From the Department of Pathology, Laboratory of Experimental Neurology; the Psychiatric Division, and the Neurological Division of the Bellevue Hospital.

1. Wortis, S. B.: Bull. Neurol. Inst. New York **4**:588 (April) 1936.

2. Greenberg, L. D.; Rinehart, J. F., and Phatak, N. M.: Proc. Soc. Exper. Biol. & Med. **35**:135 (Oct.) 1936.

3. Plaut, F., and Bülow, M.: Ztschr. f. physiol. Chem. **236**:241, 1935.

4. Plaut, F., and Bülow, M.: Klin. Wchnschr. **14**:276 (Feb. 23) 1935.

5. Footnote deleted on proof.

6. Plaut, F., and Bülow, M.: Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:481, 1936.

7. Wright, I. S.: Am. J. M. Sc. **192**:719 (Nov.) 1936; Proc. Soc. Exper. Biol. & Med. **32**:475, 1934. Wright, I. S., and Lilienfeld, A.: Pharmacologic and Therapeutic Properties of Crystalline Vitamin C (Cevitamic Acid), with Especial Reference to Its Effects on Capillary Fragility, Arch. Int. Med. **57**:241 (Feb.) 1936.

The vitamin C content of the spinal fluid varies with the age of the subject, decreasing as he grows older. According to the work of Plaut and Bülow,[8] persons between 20 and 35 years of age have 1.77 mg. per hundred cubic centimeters; those between 36 and 59, 1.97 mg., and those between 61 and 83, 0.51 mg. Our figures are somewhat higher (table 1). This discrepancy, we believe, is due to the difference between the American and the Continental dietary, and perhaps to slight differences in method.

The difference between the vitamin C content of the diet of young and that of old persons probably does not account for the differences in the amount of vitamin C in the spinal fluid. Furthermore, this quantitative difference is not entirely due to defective absorption in older persons, for after oral administration of vitamin C the content of the spinal fluid rises as it does in younger persons. The conclusion is therefore tenable that the lower values for vitamin C in the spinal fluid of

TABLE 1.—*Vitamin C Content of Cerebrospinal Fluid* in Normal Persons*

Age, Years	Plaut and Bülow, Mg. per 100 Cc.	Our Figures, Mg. per 100 Cc.
20-35	1.77	2.64
36-59	1.97	2.53
61-83	0.51	....

* The method of Farmer and Abt (Proc. Soc. Exper. Biol. & Med. **32**: 1625, 1935) was used in determining the vitamin C content of cerebrospinal fluid.

older persons may be due to decreasing intensity of the metabolic processes concerned with the elaboration of vitamin C.

Febrile diseases decrease the vitamin C content of the spinal fluid.[9] This is probably due to the fact that fever increases the body metabolism and that there is therefore greater utilization of vitamin C. The validity of this finding has been confirmed by Mosonyi,[10] who remarked that the daily administration of thyroxin to guinea pigs markedly reduces the vitamin C content of the liver and adrenal glands.

It has also been observed that there is no change in the vitamin C content of the cerebrospinal fluid after prolonged narcosis from opium derivatives and amylene hydrate.[11]

We have found that in the normal and in the vitamin C deficient person there is an almost constant parallelism between the concentration of vitamin C in the blood and the spinal fluid and the urinary excretion

8. Plaut, F., and Bülow, M.: Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:324, 1935.
9. Plaut, F., and Bülow, M.: Klin. Wchnschr. **14**:1318 (Sept. 14) 1935.
10. Mosonyi, J.: Orvosi hetil. **80**:81, 1936.
11. Plaut, F., and Bülow, M.: Klin. Wchnschr. **14**:1716 (Nov. 30) 1935.

of this substance (i. e., the five hour excretion test[12]). Our findings correspond with and confirm those of Plaut and Bülow,[13] showing that the vitamin C content of the cerebrospinal fluid is an accurate index of the relative concentration in the body.

STUDIES ON TISSUE EXTRACTION

Vitamin C is present in relatively high concentrations in nerve tissue, the highest being found in the adrenal, the brain[14] and the pars intermedia of the hypophysis.[15] Mělka[16] reported the cevitamic acid content of the cerebellar cortex, the cerebral cortex, the globus pallidus and the corpus callosum to be, respectively, 0.26, 0.17, 0.16 and 0.13 mg. per gram of tissue. Peripheral nerves, however, contain only 0.03 mg. per gram of tissue. Malmberg and von Euler[17] found (1) that cevitamic acid occurs in the brain mostly in the reduced form, (2) that it is present in greater amounts in the brain of the young animal and (3) that the quantity diminishes in scorbutic guinea pigs to about one fifth of the normal. They concluded that the high respiratory rate of brain tissue, particularly that of young animals, probably has something to do with its relatively high cevitamic acid content.

Guinea pigs weighing from 200 to 500 Gm. were used in our experiments. The guinea pig is suitable for these experiments, since it does not synthesize vitamin C, as do some animals. In this respect it is similar to man, who likewise cannot synthesize this substance; moreover, scurvy in man and that in the guinea pig show similar pathologic changes.[18] The vitamin C contents of six different tissues, namely, adrenal, brain, spleen, liver, kidney and heart, were determined for both normal and scorbutic animals (table 2). In the normal guinea pigs the spleen (in three determinations) contained somewhat higher concentrations of vitamin C than did the brain, a finding which is not in keeping with that of other workers. The concentrations of vitamin C in tissues of normal guinea pigs in the order of decreasing amounts were those in the adrenal, spleen, brain, liver, kidney and heart. Since only three determinations were made on spleen, this finding may be subject to revision. This, how-

12. Wright, I. S.; Lilienfeld, A., and MacLenathen, E.: Determination of Vitamin C Saturation: A Five Hour Test After an Intravenous Test Dose, Arch. Int. Med. **60**:264 (Aug.) 1937.

13. Plaut, F., and Bülow, M.: Ztschr. d. ges. Neurol. u. Psychiat. **154**:481, 1936.

14. Wortis, H.; Wortis, S. B., and Marsh, F. I.: Unpublished data.

15. Glick, D., and Biskind, G. R.: J. Biol. Chem. **110**:113 (Aug.) 1935.

16. Mělka, J.: Arch. f. d. ges. Physiol. **237**:216, 1936.

17. Malmberg, M., and von Euler, H.: Chem. Abstr. **29**:7401, 1935.

18. Wolbach, S. B.: Pathologic Changes Resulting from Vitamin Deficiency, J. A. M. A. **108**:7 (Jan. 2) 1937.

ever, was not true for scorbutic guinea pigs. The concentrations in the order of diminishing amounts occurred in the adrenal, brain, liver, spleen, kidney and heart. The percentage decrease of vitamin C in the scorbutic animals was highest in the adrenal glands (86) and diminished in the spleen, liver, brain, kidney and heart, respectively. Studies on the vitamin C content of human tissues gave similar results.[19]

It is therefore apparent that nerve tissue is one of the large reservoirs of vitamin C in the body.

IMMUNOLOGIC STUDIES

Jungeblut [20] demonstrated that extraordinarily small amounts of vitamin C are capable of inactivating multiple paralytic doses of poliomyelitis virus in vitro. He maintained that there is a remarkable similarity

TABLE 2.—*Vitamin C Content of the Blood and of Six Tissues of Normal and Scorbutic Guinea Pigs*

Animals	Blood, Mg. per 100 Cc.	Adrenal, Mg. per Gm.	Brain, Mg. per Gm.	Spleen, Mg. per Gm.	Liver, Mg. per Gm.	Kidney, Mg. per Gm.	Heart, Mg. per Gm.
Normal, 6	0.77 (0.42-1.08)	0.77 (0.40-1.12)	0.23 (0.13-0.29)	0.30 (0.20-0.39)	0.20 (0.12-0.36)	0.13 (0.08-0.23)	0.075 (0.04-0.12)
	6 determinations	6 determinations	6 determinations	3 determinations	6 determinations	5 determinations	5 determinations
Scorbutic, 10	0.30 (0.23-0.46)	0.11 (0.05-0.18)	0.08 (0.04-0.10)	0.05 (0.032-0.07)	0.06 (0.04-0.086)	0.048 (0.03-0.066)	0.03 (0.017-0.049)
	5 determinations	10 determinations	10 determinations	10 determinations	8 determinations	8 determinations	10 determinations
Percentage decrease	61	86	65	83	70	62	60

between the quantitative aspects of this inactivation and the neutralization of diphtheria toxin by vitamin C. It is therefore noteworthy that two such heterogeneous substances as diphtheria toxin and poliomyelitis virus, the one a lifeless poison and the other a presumably living agent, should prove susceptible to the inactivating power of no less than three highly reducing substances; i. e., epinephrine, extract of adrenal cortex and vitamin C, all of which are present in the adrenal gland. Further work may provide a common basis for the biochemical reactions involved. It is pertinent that the amounts of vitamin C present in the central nervous system are well within the range which Jungeblut found to be neutralizing. He added [21] that he has obtained "definite therapeutic results from the administration of vitamin C to poliomyelitic monkeys"

19. Yavorsky, M.; Almaden, P., and King, C. J.: J. Biol. Chem. **106**:525 (Sept.) 1934.

20. Jungeblut, C. W.: J. Exper. Med. **62**:517 (Oct.) 1935.

21. Jungeblut, C. W.: Personal communication to the authors.

and suggested that "these are accomplished by a critical change in the oxidation-reduction potential in the nervous tissue; this would prevent multiplication of the virus, which is known to be highly vulnerable to oxidizing agents." Further clinical work along these lines is, of course, indicated before the experimental work of Jungeblut can be accepted as having human application.

PATHOLOGIC STUDIES

Although there are many reports in the literature on neurologic and mental changes accompanying scurvy,[22] no proof has been given that the neuropsychiatric sequelae are the specific result of deficiency of vitamin C in the diet. The only careful study we are aware of is that by Davison.[23] He placed seven guinea pigs on a diet free from vitamin C;

TABLE 3.—*Vitamin C Content of Blood and Brain; Respiratory Quotient and Oxygen Consumption of the Cortical Gray Matter of the Brain of Normal and Scorbutic Guinea Pigs*

Animals; Weight, Gm.	Vitamin C Content		Respiratory Quotient		Oxygen Consumption, Cu. Mm. per Mg. of Tissue (Wet Weight)			
					Plain Ringer-Phosphate Solution, p_H 7.4		Ringer-Phosphate Solution, p_H 7.4, with 0.2 per Cent Dextrose	
	Blood, Mg. per 100 Cc.	Brain, Mg. per Gm.	Plain Ringer-Phosphate Solution, p_H 7.4	Ringer-Phosphate Solution, p_H 7.4, with 0.2 per Cent Dextrose	60 Min.	120 Min.	60 Min.	120 Min.
Normal (3) 400-500 Gm.	1.04 (0.80-1.46)	0.29	1.07	0.98	0.72	1.38	0.99	1.83
Normal (6) 250-350 Gm.	1.03 (0.93-1.08)	0.22 (0.20-0.24)	0.97	1.00	0.81	1.49	0.98	1.92
Scorbutic (7) 190-350 Gm.	0.29 (0.23-0.40)	0.08 (0.047-0.094)	1.01	1.00	0.81	1.45	1.04	2.09

clinical signs of scurvy developed in all. Of this number two presented terminal neurologic signs, consisting of alternating flexion and extension movements and dragging the hindlimbs. Pathologically, the peripheral nerves of these animals showed slight disintegration of myelin, and on rare occasions destruction of the axis-cylinders. In addition, the various nerve cells, especially those of the anterior horn, disclosed pathologic changes, such as vacuolation, liquefaction necrosis, swelling and pyknosis. Davison, however, noted similar pathologic changes in guinea pigs that were totally starved. He concluded that none of the histopathologic changes observed could be attributed specifically to avitaminosis C. We have not, as yet, completed the pathologic study of our material. At

22. Hess, A. F.: J. Infect. Dis. **23**:438 (Nov.) 1918. Stewart, R. M.: J. Neurol. & Psychopath. **6**:191 (Nov.) 1935. Kennedy, F., and Wortis, H.: Surg., Gynec. & Obst. **63**:732 (Dec.) 1936.

23. Davison, C.: Personal communication to the authors.

autopsy a constant observation in the animals was hypertrophy of the adrenal gland. The significance of this change is not yet clear to us, but it seems to indicate an intimate relationship between the adrenal gland and vitamin C metabolism.

An important observation which may have related significance is that of Kuchel and Mitchell,[24] who observed diminution in the cevitamic acid content of the adrenal gland as a result of electrical stimulation and fear.

STUDIES ON BRAIN METABOLISM

The Barcroft-Warburg technic for the study of tissue metabolism has been used by us and is described elsewhere.[25] Its application to study of the effects of vitamin deprivation on the metabolism of nerve tissue is relatively recent. Peters, Sinclair and Thompson [26] showed that there is defective oxidation of nerve tissue in animals with avitaminosis B_1 and, furthermore, that the addition of vitamin B_1 to such tissues produces an increase to normal in the brain and nerve tissue respiration. In addition, Himwich and his co-workers [27] and Joly [28] demonstrated defects in the brain metabolism of similarly deprived animals in the nature of diminished ability to oxidize lactic acid, with resultant diminution in the respiratory quotient below unity, which obtains in normal animals.

Studies already completed indicate therefore that there is a definite relationship between vitamin B_1 and carbohydrate metabolism in general and, more specifically, between vitamin B_1 and the transformation and removal of two important catabolites of carbohydrate metabolism, namely, lactic and pyruvic acid. If one recalls that carbohydrate is the usual nutritive substance of nerve tissue,[29] the importance of such a finding becomes apparent.

In an attempt to evaluate the effects of vitamin C deprivation on metabolism of brain tissue, the respiratory quotient and oxygen consumption of the cortical gray matter in nine normal and seven scorbutic guinea pigs were measured. The results were then tabulated and correlated with the vitamin C content of the blood and of the brain (table 3). The data indicate the following:

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24. Kuchel, C. C., and Mitchell, M. L.: Australian J. Exper. Biol. & M. Sc. **14**:51 (March) 1936.

25. Wortis, S. B.: Am. J. Psychiat. **93**:87 (July) 1936.

26. Peters, R. A., and Sinclair, H. M.: Biochem. J. **27**:1677, 1933. Peters, R. A., and Thompson, R. H. S.: ibid. **28**:916, 1934.

27. Himwich, H.; Fazikas, J. F.; Rakisten, N., and Sanders, R.: Proc. Soc. Exper. Biol. & Med. **30**:903 (April) 1933.

28. Joly, J. M.: Compt. rend. Soc. de biol. **122**:196, 1936.

29. Wortis, S. B., in Nelson Loose Leaf Living Medicine, New York, Thomas Nelson & Sons, 1935, vol. 6, p. 117.

1. The level of vitamin C in the blood of scorbutic guinea pigs is about 30 per cent of that of normal animals.

2. The cortical gray matter of the brain of scorbutic guinea pigs contains only from one third to one sixth as much cevitamic acid as does similar tissue from the animals used as controls.

3. The respiratory quotient of excised brain tissue (cortical gray matter) is unity, or close to unity, in both normal and scorbutic guinea pigs, indicating the oxidation of dextrose or lactic acid.

TABLE 4.—*Vitamin C Studies on Normal and Chronic Alcoholic Persons*

Diagnosis	Findings for Vitamin C*		
	Blood, Mg. per 100 Cc.	Spinal Fluid, Mg. per 100 Cc.	Age in Years
Normal persons	0.6-1.3 (method of Farmer and Abt)	2.64	20-35
		2.54	36-59
		—	61-83
Chronic alcoholic patients (total 92)			
1. Without psychosis or peripheral neuritis (9)	0.64†	2.78	20-35
		2.86	36-59
		2.41	61-83
2. With peripheral neuritis (8)	0.37	1.10	20-35
		0.82	36-59
3. Alcoholic hallucinosis with mild peripheral neuritis (10)	0.27	0.61	20-35
		0.88	36-59
4. Alcoholic hallucinosis (35)	0.33	0.80	20-35
		0.67	36-59
		0.53	61-83
5. Alcoholic hallucinosis following recovery (6)	0.38	1.27	20-35
		1.69	36-59
6. Delirium tremens (14)	0.29	0.96	20-35
		0.77	36-59
		1.14	61-83
7. Korsakoff's psychosis (5)	0.28	1.07	36-59
		0.55	60-83
8. Alcoholic encephalopathy (5)	0.30	0.66	20-35
		0.91	36-59

* All figures given are average values unless otherwise noted.
† Values for chronic alcoholic patients in this column are expressed as averages for all age groups.

4. The oxygen consumption of the cortical gray matter of the brain of the guinea pig is (within the limits of experimental error) the same in both the normal and the scorbutic animal.

5. The oxygen consumption of the brain in normal heavy (old) guinea pigs is less than that of similar tissue in young animals.

CLINICAL STUDIES

Studies on the vitamin C content of the blood and the cerebrospinal fluid were made on a large group of normal persons and on ninety-two patients with chronic alcoholism [30] (table 4). The results were as follows:

30. Wortis, H.; Wortis, S. B., and Marsh, F. I.: Am. J. Psychiat. **95**:891, (Jan.) 1938.

1. Chronic alcoholic persons without psychosis or peripheral neuritis have a normal vitamin C content of the blood and the cerebrospinal fluid.

2. Alcoholic persons with peripheral neuritis or alcoholic psychopathy have a subnormal vitamin C content of the blood and the cerebrospinal fluid.

The possible significance of these findings has been discussed at length in a previous communication.[30] The results justify the assumption that there is a nutritional factor in the production of gross mental and nervous changes in persons with chronic alcoholism.

CONCLUSIONS

The more recent work relative to the role that vitamin C may play in the functioning of the nervous system has been reviewed.

It is suggested that vitamin C probably plays a role in the metabolism of nerve tissue, for the following reasons:

1. It is present in relatively large amounts in the cerebrospinal fluid.

2. Work on tissue extraction reveals that the adrenal, brain and pars intermedia of the hypophysis (all nerve tissues) are great body reservoirs for this substance.

3. Scorbutic animals show hypertrophy of the adrenal gland.

4. Jungeblut has shown that vitamin C has definite protective and therapeutic value in experimental poliomyelitis.

5. Clinical studies show that in alcoholic conditions associated with neural or mental changes there are subnormal levels of vitamin C in the blood and cerebrospinal fluid.

Drs. Karl M. Bowman and Foster Kennedy, directors of the psychiatric and neurologic services, respectively, of Bellevue Hospital, permitted use of the clinical material.

DISCUSSION

DR. FOSTER KENNEDY, New York: I should like to emphasize that the appearance of this kind of work is an indication of a new wind blowing in pathology—that pathology of the past has been largely confined to what could be seen by the microscope and that the important pathology of the future will perhaps have no visible form.

That the younger men are reporting on chemical and metabolic studies, investigations on uses of the vitamins and on the function or role of enzymes in nervous reactions, shows that pathology is advancing to new ideologic levels.

The citation made by Dr. Wortis to the work of Jungeblut on the value of vitamin C in inactivation of the poliomlyelitic virus shows that it may have a protecting influence in the prevention of injury to nerve tissues. The role played normally by the adrenal glands as a protector of nerve tissue is also demonstrated.

I do not know from Dr. Wortis' statement whether the great reduction in vitamin C in his chronic alcoholic patients may not be due to a difference in the diet of alcoholic patients suffering from encephalopathies and that of alcoholic patients in whom there is no mental or cerebral change. I do not know whether

the great reduction in the vitamin C of the cerebrospinal fluid may not be due to the environmental and dietary situation.

DR. EMANUEL FRIEDMAN, New York: I wish to add my praise of the work which was involved in the preparation of this paper.

One seems today to be under the shadow, or shall I say the light, of the vitamins. All are cognizant of the fact that vitamin B plays an important role in the genesis of neural disease. The work presented today indicates that possibly vitamin C also is concerned in neurophysiologic disturbances.

The fact that vitamin C is particularly abundant in the adrenal cortex and the pituitary gland seems to point to its significance in sugar metabolism. It is known that the adrenal is an important center for the control of sugar metabolism, particularly because of its influence on the sympathetic nervous system, stimulation of which gives rise to mobilization of sugar in the sense propounded by Cannon. The pituitary gland, too, is concerned with sugar metabolism, through its connection with the tuber cinereum.

It seems that carbohydrate metabolism is influenced considerably by deprivation of vitamin C because there is progressive decrease in the ability of the organism to dispose of absorbed sugar. In the experimental animal this becomes evident after ten days of deprivation. In the older studies on scurvy it was indicated that the loss of weight during the development of acute scurvy was due possibly to inanition. From the work that was presented here, it seems that possibly the difficulty may lie also in deprivation of vitamin C, with its effect on absorbed carbohydrate.

Dr. Wortis has stated that the vitamin C content of the spinal fluid decreases as one grows older, owing to slowing up of the metabolic process. I venture to make a different suggestion, namely, that in older persons there is less need for vitamin C because the processes of anabolism are no longer so essential. This view seems to be borne out by the fact that increased utilization of vitamin C is associated with fever, with its acceleration of the metabolic process, and with increase in metabolism which has been produced by administration of thyroxin. In other words, acceleration of carbohydrate metabolism seems to be dependent on the presence of adequate amounts of vitamin C.

The high respiratory rate of brain tissue, especially in young animals, to which the authors refer, might be explained by the need for oxygen of the growing brain. The brain tissue is highly sensitive to anoxemia, particularly in its immature states—hence the need for rapid oxidation and reduction reactions, which are dependent on an adequate supply of vitamin C.

I shall not refer to the work of Jungeblut because Dr. Kennedy has already done so, except to say that it seems that deficiency in vitamin C does not interfere materially with the formation of antibodies but does impair the effectiveness of immunization of the experimental animal to tetanus or diphtheria.

The only references to neural lesions in cases of vitamin C deficiency that I was able to find in a survey of the literature were those made by Davison in the experimental animal. He himself, however, is not yet convinced that the lesions are due to the absence or deficiency of vitamin C.

The hypertrophy of the adrenals to which Dr. Wortis has referred is suggestive, for many years ago, if my memory serves me correctly, it was noted as a pathologic and anatomic fact that in an anencephalic monster there is a tendency to hypertrophy of the adrenals. It seems that the adrenal cortex becomes overactive and stores lipoids as compensation for the deficiency of lipoids in the brain.

Does Dr. Wortis believe that there is a parallelism between deficiency in vitamin B and that in vitamin C in neural disease? I ask this question because I have had the opportunity to observe four cases of avitaminosis associated with neural lesions (three cases of polyneuritis and one of dorsolateral sclerosis) in none of which vitamin C studies indicated any deviation from the normal.

Dr. Abraham Myerson, Boston: Concurrent with Dr. Wortis' research, an investigation has been carried out with the Pijoan method by my colleagues and me in the laboratory of the Boston State Hospital and by Dr. Pijoan himself on the cevitamic acid content of the blood in elderly persons and in alcoholic patients. Our figures differ from those obtained by Dr. Wortis, but the main facts are the same, namely, that in the old patients, those of 65 and over, there is a sharp reduction in the cevitamic acid of the blood serum and that in the alcoholic patients there is a marked reduction, even below that shown by the senile patients. In the patients with alcoholic psychoses, especially those associated with neuritis, the vitamin C content is decidedly low, and in old persons there is a diminution. In a patient who has lived in the state hospital for many years and who presumably has had a fair diet but gets little exercise the vitamin C content is intermediate between the senile and the normal value. Our results on the whole substantiate the facts presented here.

Dr. Ernest Sachs, New York: I should like to ask Dr. Wortis what he found when he made good the deficiency in vitamin C.

Dr. Israel Strauss, New York: This work is important, but I am afraid that clinically one should not lay too much stress on the deficiency of any particular vitamin.

Recently, I had occasion to observe two persons who had little in the way of symptoms referable to the nervous system—practically nothing objective. In one patient there were simply constant paresthesia and burning in the limbs. One would immediately think of the possibility of the neural symptoms of pernicious anemia, with the beginning of dorsolateral sclerosis. The man was a bar-tender, who drank freely but who, on careful inquiry, was found to have eaten an extremely well balanced diet. Examination of the spinal fluid revealed deficiency of vitamin C, but that did not solve the problem. Some factor must be present to explain why a man of this type showed any symptoms referable to the nervous system. Examination of the stomach contents after injection of histamine showed absence of free hydrochloric acid. The therapeutic indication, therefore, was administration of concentrated doses of vitamins, in this case particularly B_1. He was given tomato juice with a high caloric diet and hydrochloric acid. He made a complete recovery. On the other hand, an Italian aged 55, who drank two bottles of wine at a meal and ate a great deal of cheese, complained that in the morning when he arose he could see well but that in a few hours there was definite blurring of vision, more marked in one eye than in the other. Examination of the eyes showed nothing abnormal, except a definite limitation of the color field. He had a slight lack of vitamin C in the spinal fluid, but an extremely good digestive apparatus. There was plenty of free hydrochloric acid. In this case, again, the patient received a diet high in calories and vitamins with B_1 concentrate, and made an extremely good recovery.

I do not think one can use lack of vitamin C as the only criterion of the deficiency. One must also look particularly into the absorptive power of the patient and the function of the digestive organs. It is not sufficient to take a person's word as to the balanced character of his diet.

I have not told either of these patients to abstain from alcohol, but have impressed on them the importance of keeping up the prescribed diet. The economic factor also enters into the situation, for many patients are unable to buy food in sufficient quantities and of the requisite character. The patient who lacked free hydrochloric acid was given hydrochloric acid and was told to continue to take it.

As a result of these considerations, I feel that while this kind of work is of great importance, it is necessary not to overstress oue factor and forget that there may be others of equal importance.

DR. HERMAN WORTIS: Dr. Kennedy brought up the question of diet. A dietary factor is undoubtedly present. As a matter of fact, there are probably many causes for the low figures for vitamin C that we obtained. The first is the dietary factor already mentioned. The second is the increase in total metabolism which occurs in alcoholic states. A third is the known difficulty in absorption which many alcoholic patients have. The role each factor may play in any individual case is often difficult to evaluate.

Dr. Friedman's question concerning the role of vitamins in sugar metabolism calls for comment. It is now known that vitamin B_1 is intimately related to sugar metabolism—more particularly to two important catabolites of carbohydrate metabolism, namely, lactic and pyruvic acid. Concerning the role of vitamin C in sugar metabolism nothing is known. Dr. Friedman's suggestion, however, is interesting and suggests a fertile field for further research.

With regard to the high respiratory rate in young persons: I think his thesis is at least as tenable as that offered by Malmberg and von Euler, whom we merely cited.

There are several reports in the literature on neurologic changes complicating scurvy, but the specific relationship of these changes to avitaminosis C has never been proved. Most of the cases reported are those of polyvitamin deficiency. In fact, we feel certain that in these cases lack of vitamins B and A was probably much more important in causing the neurologic changes. What we really are trying to find out is whether vitamin C has any importance in nerve tissue metabolism.

Is there a parallel relationship between lack of vitamin B and that of vitamin C? This cannot be so in all cases—if it were, all patients with low vitamin C would tend to have peripheral neuritis. It is also known that vitamin B is excreted more rapidly than vitamin C. There are, in addition, many other factors which complicate the picture and preclude at this time a satisfactory answer to Dr. Friedman's pertinent question. When people take ulcer diets they frequently acquire scurvy without any signs of peripheral neuritis because that particular diet is deficient in vitamin C but adequate in vitamin B. In alcoholic patients, on the other hand, there is evidence to show that such a parallelism may exist.

It is exceedingly encouraging to have so careful a worker as Dr. Myerson confirm our work. The difference in figures is probably accounted for by the fact that we used a different chemical technic in making our vitamin C determinations (Farmer and Abt).

Dr. Sachs' question will be answered at some time in the future—we have not reached that stage of the work. We are so certain that vitamin B is more important in relationship to the alcoholic psychoses that we believe this particular problem should be attacked first with a study of vitamin B. Such an investigation is now under way.

With Dr. Strauss' comment one can only agree. We did not mean to overstress any particular factor and I do not believe that we did. It is well known

that alcoholic patients frequently do not absorb material from the stomach and that medication must be intramuscular or intravenous. The causative factor for their symptoms is, however, the lack not of free hydrochloric acid in the stomach but of the vitamin B complex, which they cannot absorb. In a case such as was described by Dr. Strauss, in which the diet was apparently adequate, treatment was properly directed toward improving absorption from the stomach, but the symptoms were probably due to lack of vitamin B_1.

Obituaries

MICHAEL A. BURNS, M.D.
1884–1938

Dr. Michael A. Burns died on March 7, 1938, after a short illness. He was born in Philadelphia, May 23, 1884, the son of James M. and Mary A. (Rowen) Burns. His general education was obtained in the parochial schools and in the Roman Catholic High School. From the latter he received the degree of bachelor of arts. He studied medicine at the Jefferson Medical College of Philadelphia, graduated in 1907 and served an internship of sixteen months at St. Agnes Hospital. He took residence in West Philadelphia, where he practiced general medicine for several years, during which period he worked in the neurologic service of Dr. Francis X. Dercum, at the Jefferson Medical College Hospital. After Dr. Dercum's death he was associated with Dr. E. A. Strecker, whom in 1934 he succeeded as professor of nervous and mental diseases in his alma mater. He served in the World War from December 1917 to December 1918 as neuropsychiatrist to Base Hospital No. 38, and from December 1918 to June 1919 as consultant in neuropsychiatry to the district of Paris, France. He returned to the United States as a major in 1919.

From the time he resumed civilian life he vigorously applied himself to the practice of neuropsychiatry. He taught at the Jefferson Medical College; he was neurologist, neuropsychiatrist or consultant to numerous hospitals and institutions; he served as a valuable officer or member of many scientific organizations, acted as trustee of the Eastern State Hospital for the Insane at Norristown, Pa., and as a director of the Philadelphia County Medical Society. He found time to write on neurology, psychiatry and mental hygiene and to be an active member of clubs and fraternities. He was deeply, but not showily, religious. Of friends he had hosts, and once his friendship was gained it was withdrawn only for flagrant cause.

Thirty years of professional life is a short span in which to attain the record vouchsafed to Dr. M. A. Burns, but when one surveys the man from a relatively intimate association, the reason is almost self evident. Burns was not the profoundly scientific plodder. He was an excellent clinician who amplified his knowledge of the signs and symptoms of disease with an accurate mental visualization of the underlying pathologic changes. He added to these qualities a personality that engendered faith; he exhibited a meticulous interest in the general

welfare of his patients that invited recovery. Even with those he knew to be hopelessly ill he evidenced, at all times, encouraging attitudes to make their finality less fearsome.

Despite his multitudinous professional duties and engagements, he was always a family man. He married in 1910 Margaret Agnes Keenan, by whom he had two sons—Paul V., an officer in the United States Naval Air Service, and John A., a student at St. Joseph's College. The entertainment of his friends and associates was always a grand occasion. If fault he possessed, it was in the neglect of his physical health. For four or five years before his final illness he was cognizant of the threatened tragedy, but when cautioned and advised to curtail his activities, he laughed at the anxious advisers and continued on his busy way to death from disease of the coronary arteries.

Those who knew him best will miss him most. The neurologic specialty was adorned by his presence in it. The medical profession has lost a shining example of service and unselfishness.

J. W. McConnell, M. D.

Abstracts from Current Literature

Physiology and Biochemistry

On the Birefringence of Nerve Sheaths as Studied in Cross Sections. Priscilla Chinn and Francis O. Schmitt, J. Cell. & Comp. Physiol. **9**:289 (Feb.) 1937.

Owing to the concentric layer structure of the proteins of the myelin sheath of vertebrate nerves, the axons show a negative polarization cross when viewed in cross section, provided that the lipoid has first been extracted from the sheath with alcohol. A negative cross was also found in the metatropic axon sheath of giant fibers from the ventral cord of the lobster. The ultrastructures of the axon sheaths of nerves, whether vertebrate or invertebrate, are essentially similar.

Chornyak, Pittsburgh.

An Attempt to Fatigue the Melanophore System in Fundulus and a Consideration of Lag in Melanophore Responses. George Howard Parker and Helen Porter Brower, J. Cell. & Comp. Physiol. **9**:315 (April) 1937.

Long-continued normal exercise does not fatigue the melanophore system of Fundulus to any measurable extent. In this respect the activities of the melanophore system resemble those observed in nerve transmission. In many ways the melanophore system resembles that of smooth muscle. Long residence of Fundulus on a white background hastens the dark to pale response and slows the pale to dark response. It also introduces an initial lag in the pale to dark response. Long residence on a black background hastens the pale to dark response and slows the dark to pale response. It also introduces an initial lag in the dark to pale response. These peculiar changes are due to temporary storage of the blanching lipohumor and of the darkening lipohumor, respectively, and probably are exhibited by Fundulus until these extra supplies are exhausted.

Chornyak, Pittsburgh.

The Relative Respiratory Activity of Sheath and Axones in Resting Limulus Optic Nerve. Herbert Shapiro, J. Cell. & Comp. Physiol. **9**:381 (April) 1937.

The results which Guttman (1935) obtained for the intact nerve (viz., nonuniformity in oxygen uptake by different portions of the optic nerve and in general, a maximum rate along the middle of the nerve) are confirmed by these studies on the axon and the sheath individually and by measurements of whole nerves. It is shown (*a*) that the oxygen uptake by the axon is constant over a period of many hours, whereas the sheath generally shows increasing metabolism with time, after an initial period of steady activity; (*b*) that though the axon and the sheath are almost equivalent in bulk, the respiration of the axon is from four to five times that of the sheath; (*c*) that in general only the axon shows maximum activity along the middle of the nerve, which phenomenon is regarded as a property of the axon; (*d*) that the effect persists in the optic nerves of animals which have been dark adapted for periods varying from six-tenths to sixteen days, with a shift of the maximum toward the central end of the nerve, and (*e*) that temperature does not alter these relationships.

Chornyak, Pittsburgh.

Automaticity in Transplanted Anuran Lymph Hearts. Marion A. Reid, J. Exper. Zoöl. **76**:47 (May) 1937.

Lymph hearts were excised and transplanted into the sinus basihyoideus in the amphibia Bufo marinus, Rana catesbeiana and Rana pipiens. The transplanted

hearts developed spontaneous, coordinate rhythmicity and reacted to stimuli precisely as does the cardiac ventricle. Action potentials from the beating transplants showed brief phasic variations, in sharp contrast to the repetitive oscillations characteristic of the normally activated organ. No ganglion cells were observed in the transplanted lymph hearts. It is concluded that the lymph hearts exemplify, in their potentialities, a functional continuity between the skeletal and the cardiac types of musculature.

WYMAN, Boston.

THE CONTROL OF TONUS AND LOCOMOTOR ACTIVITY IN THE PRAYING MANTIS (MANTIS RELIGIOSA L.). K. D. ROEDER, J. Exper. Zoöl. **76**:353 (Aug.) 1937.

The posture, activity and general behavior of praying mantids were observed and recorded photographically in normal insects and in those in which various parts of the central nervous system were destroyed. Destruction of the eyes produced loss of the visual response and a slight decrease in activity. Destruction of one protocerebral ganglion reduced the tonus of the neck and prothoracic muscles on the side of operation resulting in postural asymmetry. There was also a great increase in locomotor activity, with circus movements toward the intact side. Destruction of both protocerebral ganglia resulted in loss of tonus on both sides and locomotor restlessness. Division of the ganglia resulted in decreased locomotor activity, hypernormal cervical and prothoracic tonus and increase in the visual responses. Locomotion was possible on strong stimulation after removal of the subesophageal ganglion. Coordinated stepping and tarsal grasping disappeared after separation of the mesothoracic and metathoracic ganglia.

It was concluded that the thoracic ganglia control locomotor coordination and that a center in the subesophageal ganglion can excite locomotor activity on stimulation. The protocerebral ganglia inhibit this subesophageal locomotor center and maintain the tonus of the neck and prothoracic muscles by excitation. These protocerebral centers discharge spontaneously and have strictly homolateral control. Their activity is diminished by inhibitory impulses from the contralateral ganglion and increased by homolateral sensory impulses.

WYMAN, Boston.

FURTHER OBSERVATIONS UPON GRASPING MOVEMENTS AND REFLEX TONIC GRASPING. F. M. R. WALSHE and J. H. HUNT, Brain **59**:315, 1936.

Observations recorded by Walshe and Robertson (1933) led them to conclude that in the phenomenon known as "forced grasping" there are two distinct and separable components. These are (1) volitional grasping movements in response to objects seen or contacts felt in the palm of the hand and (2) reflex tonic grasping in response to stretching the flexor muscles of the fingers.

Another series of cases has since been investigated by Walshe and Hunt with a view to studying separately the visual, tactile and proprioceptive factors. For this purpose, use was made of the method of blocking the cutaneous—median, ulnar and radial—nerves to the hand with procaine hydrochloride. The hand was thus rendered anesthetic and the tactile factor excluded. If, in addition, the patient was blindfolded, vision was also excluded, and the factor of stretch could be observed in isolated operation.

In a case of hemiparesis, when the hand was anesthetized, grasping movements were obtained with the eyes open but were absent with the eyes blindfolded. Reflex tonic grasping was wholly unimpaired in intensity, despite the insensitiveness of the skin of the hand. The patient exemplified the fact that reflex tonic grasping has as its sole adequate stimulus stretch of the flexor muscles of the fingers and that it persists unimpaired when both visual and tactile stimuli are eliminated. The primacy of physiologic factors in the causation of grasping movements was also illustrated. Fulton (1934), however, maintained that these volitional movements are as wholly reflex as the invariable tonic grasping which persists even in

the unconscious patient. He took this position by virtue of his belief that "the one fundamental tenet in the creed of modern neurophysiology" is the reflex nature of all possible movements.

It was emphasized by Walshe and Robertson (1933) that the patient with "forced grasping" can open his clenched fist easily when it is empty, and even when it contains an object which is not being pulled away so that there is stretch on the flexor muscles of the fingers. Occasionally a subject may appear to have more or less difficulty in relaxing the grasp of his empty hand. This apparent exception to the general rule does not necessitate any revision of the authors' view as to the cause of tonic grasping, which is, in their experience, always due to intervention of other factors. Of these apraxia is perhaps the most important, and the inability of the patient with reflex tonic grasping to open his empty fist on request is commonly due to apraxia. The presence of apraxia has no influence on reflex tonic grasping in response to stretch. These facts were illustrated by Walshe and Hunt in three cases.

Perhaps less striking is the influence of hypertonus of the grasping limb. If any degree of spasticity involves the limb which shows grasping movements there is increased delay in the voluntary relaxation of the clenched and empty fist, but this is a function of spasticity and impaired power of movement, and not of the grasping movement itself.

Occasionally, in a case of residual hemiplegia associated with extreme spasticity in which there is no trace of grasping movements of the kind under consideration, the permanent hypertonus of the flexor muscles of the fingers may be felt to be appreciably increased by sudden passive extension of the fingers. This increased flexor tonus is undoubtedly a response to stretch, and as such presumably is allied to the reflex tonic grasping under consideration. However, reflex tonic grasping may be fully developed and powerful in the absence of any resting hypertonus in the affected muscles and therefore cannot be regarded merely as an expression of hypertonus.

Fulton (1934) and Fulton and Bieber (1935) reported that after bilateral excision of cortical areas 4 and 6 in the monkey forced grasping varied with the animal's position in space. Kennard, Viets and Fulton (1932) reported that in the human subject the strength of the grasping phenomena varied with variation in the patient's position in space, exactly as was described for the monkey. From this they concluded that "the grasp is part of the righting reflex mechanism peculiar to primates."

With regard to this interaction in man, no trace of influence of body posture in relation to space or of head posture in relation to the trunk on either grasping movements or reflex tonic grasping could be found in any of the authors' cases.

SALL, Philadelphia.

Neuropathology

SUBACUTE NECROTIC ENCEPHALOMYELITIS. RISER, GERAUD and PLANQUES, Rev. neurol. **67**:455, 1937.

In previously reported cases of necrotic myelitis the spinal cord was observed to be exclusively or almost exclusively involved. Riser and his associates describe a case of typical necrotic myelitis with marked involvement of the meninges and the cerebrum. A man aged 29 experienced generalized erythema eight days after an injection of tetanus antitoxin. Shortly afterward he began to complain of slowly progressive paraparesis. On examination one year later there was spastic paraplegia, with plantar extension bilaterally, abolition of vibratory sensation in the lower extremities, difficulty in urination and slight lateral nystagmus, with no other signs of cerebellar involvement. The eyegrounds were normal. Examination of the spinal fluid revealed 30 lymphocytes, 200 mg. of protein per hundred cubic centimeters, a doubtful Wassermann reaction and a negative reaction to the benzoin test. The Wassermann reaction of the blood was negative. In spite

of treatment with pentavalent arsenicals and iodides, the paraplegia progressed steadily. All deep and discriminatory sensation disappeared in the lower extremities, and hypesthesia to heat and pain finally appeared. Sphincter disturbances became more severe. Roentgenography with iodized poppy-seed oil showed a festooned image at the level of from the eighth cervical to the first and second thoracic vertebrae, suggesting arachnoiditis. Roentgen therapy and a decompression operation gave no relief. Flaccid tetraplegia supervened, and the patient died in decubitus two years and seven months after onset of the disease. There were plaques of leptomeningeal thickening over the hemispheres and dense spinal arachnoiditis, most marked in the cervical region. In the lower thoracic and lumbar regions was a central syringomyelic cavity, surrounded by gliosis. Central softening was observed in the upper thoracic and cervical portions of the cord. Microscopically, the softened areas were necrotic. Extensive demyelination was present about these areas as well as about the cavity. Surrounding the fine arterioles of the cortex were small old and recent hemorrhages. The ganglion cells were rarefied. In many places 50 per cent of the pyramidal cells were lost. Hemorrhages were also seen in the basal ganglia and the brain stem, but not in the spinal cord. Large vessels in the spinal cord and, to a lesser extent, in the pia were fibrotic and thickened, the thickening involving chiefly the media. The lumen was often narrowed. The arterioles were infiltrated with round cells and were hyperplastic or fibrosed. The capillaries were everywhere intact. The vascular lesions differed from those of Foix and Alajouanine in the more moderate hyperplasia and the integrity of the veins. The parenchymal lesions were more extensive than could be accounted for by ischemia alone. A virus infection is considered as the probable cause of the condition.

LIBER, New York.

CASE OF PACHYMENINGITIS CERVICALIS HYPERTROPHICANS GUMMOSA. H. BERTHA and M. FOSSEL, Monatschr. f. Psychiat. u. Neurol. **95**:102 (March) 1937.

A woman aged 45 complained of pain and numbness in the extremities and weakness of the legs after removal of an ovarian cyst. The Wassermann reaction of the spinal fluid was positive. Examination revealed: Argyll Robertson pupils; increased tendon reflexes, more marked in the left than in the right lower extremity; hypesthesia in the hands; a Babinski sign on the left, and slight ataxia of the arms and legs. The Wassermann reaction of the blood was negative. The patient was given mercury, bismuth and neoarsphenamine, but no improvement followed. Later she showed increasing weakness of the extremities and a Babinski sign bilaterally. Fluid taken at this time by lumbar puncture exhibited an increased amount of protein, a colloidal gold curve of 1123332111 and a positive Wassermann reaction. The fluid obtained on suboccipital puncture was normal in all respects. Injection of iodized poppy-seed oil disclosed complete blockage of the subarachnoid space in the upper cervical region. The patient was given malarial therapy; shortly afterward, erysipelas developed, and the patient died. Postmortem examination revealed syphilitic aortitis and chronic inflammatory changes in the meninges of the entire spinal cord. The alterations were most pronounced in the dura over the cervical region, where there was a caseating gummatous lesion. Two explanations are advanced to account for the observation that the Wassermann reaction of the fluid below the cervical lesion was positive and that above negative. 1. The colloidal substances responsible for a positive reaction may have been present in the blood in insufficient amounts to be detected, but have become concentrated in the lumbar spinal fluid, owing to altered meningeal permeability below the obstruction. 2. The colloidal substances may have been produced locally. The fact that the fluid below the obstructive lesion contained material which was not present elsewhere supports the view that the whole pial vascular system contributes to the formation of cerebrospinal fluid.

ROTHSCHILD, Foxborough, Mass.

FORMATION OF THE SENILE PLAQUE. E. A. D. E. CARP, Psychiat. en neurol. bl. **41**:201, 1937.

The nature of the senile plaque is still unknown. Some authors have stressed the importance of the microglia in its formation, and others, that of the macroglia. The present paper confirms both these concepts with regard to the formation of the external layers of the plaque. Simchowicz expressed the belief that the fundamental process is a degeneration of the finest nerve structures, followed by precipitation of abnormal products of metabolism on the neurencytium of Held. Carp has demonstrated that the structures of the plaque around the amorphous core are in close relation to the neural syncytium. This structure, unstainable under normal conditions, becomes visible when impregnated by the characteristic substances of the plaque.

LEWY, Philadelphia.

A HITHERTO UNKNOWN FORM OF INFANTILE AMAUROTIC IDIOCY. MAX BIELSCHOWSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:321 (April) 1936.

Bielschowsky reports the case of a Dutch child of non-Jewish parentage who died at the age of 2 years and 3 months. Birth was normal. Nothing unusual was observed during the first few months of life, except that at the age of 6 months the child could take only fluids. At this time it was also noted that the infant was unusually quiet, paid no attention to its surroundings and showed no spontaneous reactions. There were general hypertonicity and hyperreflexia. A Babinski sign was obtained only on the right side. Athetoid movements were often seen in the upper limbs. A cherry-red spot was not found; the disks were not pale, and the pupils reacted well to light.

Autopsy revealed that the brain was small and weighed less than normal. The ganglion cells showed the lipoid deposits characteristic of amaurotic family idiocy. Corkscrew-like dendrites were present in some of the affected ganglion cells. These are rare in cases of Tay-Sachs' disease and are seen more often in association with chronic diseases later in life. The typical cellular swelling was absent. Most of the diseased ganglion cells were smaller than normal. They did not stain with hematoxylin but appeared light orange in sudan III and scarlet red preparations. This staining reaction is usual in cases of late infantile and juvenile amaurotic family idiocy. The characteristic status spongiosus of the deeper layers of the cerebral cortex was observed. This is due to an increase in astrocytes, which is not extensive enough to replace completely the degenerated ganglion cells. The most unusual observation in this case was the large number of foci of demyelination in various parts of the central nervous system. There was no glial reaction in these areas. The axis-cylinders seemed intact. Bielschowsky believes that the condition is due to defective myelination rather than to degeneration.

SAVITSKY, New York.

CEREBRAL CHANGES IN A CASE OF WINIWARTER-BÜRGER DISEASE. MAX BIELSCHOWSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:329 (April) 1936.

Bielschowsky reports the case of a woman aged 38 who had had vasomotor changes in the extremities since the age of 28. Right hemiparesis and impairment of speech developed after an intestinal operation. In a few months she improved. After an epileptic attack the speech difficulty became much worse. She died after a second convulsion. The Wassermann reactions of the blood and spinal fluid were negative. The blood showed lymphocytosis.

Autopsy revealed that the left cerebral hemisphere was smaller than the right. There was extensive scarring in the distribution of the left anterior cerebral artery, involving mainly the medial surface and extending over the upper part of the lateral aspect of the hemisphere. There were gross changes also in the third frontal and first temporal gyri on the right side, in the distribution of the sylvian artery. The changes on the right side appeared dark and granular, owing to the presence of numerous dilated blood vessels filled with thrombi. The pres-

ence of complete secondary degeneration of the right pyramidal tract confirmed the opinion that the extensive lesion in the left hemisphere was of long standing.

Section through the altered part of the right hemisphere showed relatively fresh changes. There was an increase in the number of small veins and capillaries. The walls of these vessels showed marked proliferation of the endothelial cells. Thrombi were seen in many of the vessels. Recanalization in some of the thrombi ruled out postmortem changes. Occasional lymphocytes and histiocytes were seen in the adventitia of the larger vessels of the leptomeninges. There were numerous fat-laden Hortega cells and fibroblasts. Bielschowsky notes the remarkable limitation of the pathologic process to the second and third layers of the cortex, with sparing of the deeper parts.

Bielschowsky believes that the granular appearance of the cortex is due to the unequal intensity of the vascular changes in the various parts of the brain. The absence of anatomic evidence of inflammatory change makes it necessary to reject the designation thrombo-angiitis obliterans for this condition. The author suggests the term angiopathia proliferativa as more fitting. He favors the theory of the existence of a constitutional factor in this disease, associated with a ready tendency of the blood to clot.

SAVITSKY, New York.

Psychiatry and Psychopathology

THE BLOOD FAT IODINE NUMBER, PRESENTING EXPERIMENTAL BASIS FOR EXACT DIFFERENTIAL DIAGNOSTIC PROCEDURE. ARTHUR T. BRICE, Am. J. Psychiat. **92**:1123 (March) 1936.

The high proportion of fat in the brain suggests that disturbance in lipoid metabolism may occur in significant alterations of cerebral function. It is known that fats are involved primarily in releases called "expenditures of emotional energy" and that patients with mental diseases in a state of exaltation show higher levels of fat in the blood than comparable groups in a state of apathy. The extent to which fat reserves are called into use by the organism is measured by the iodine number of the fat in the blood. In a group of schizophrenic and a group of manic patients, each receiving identical diets, Brice found the mean iodine number to be 107 for patients with dementia praecox and 126 for those with manic excitement. The difference between the means was more than three times the standard error of the difference, so that it would appear that the results are statistically significant of a higher iodine number of the blood fat in cyclothymic than in schizophrenic patients. Brice suggests that determination of this index may be a valuable procedure for clarifying the diagnosis in cases in which there is disagreement of opinion.

DAVIDSON, Newark, N. J.

THE ECOLOGICAL PRINCIPLE IN MEDICINE. SMITH ELY JELLIFFE, J. Abnorm. & Social Psychol. **32**:100 (April-June) 1937.

Haeckel, in 1869, first popularized the word ecology and defined it as "the study of the relation of the animal to its organic as well as its inorganic environment, particularly its friendly or hostile relations to those animals or plants with which it comes in contact." In more modern phraseology, ecology can be said to be the study of the "adaptation of man as a whole to the whole of the cosmos." As an example, it is well known that habitat plays a large part in the admittedly bad teeth of many persons using water and food products drawn from chalky soils, notably in certain parts of England.

The ecologic principle demands information of a total quality. It is not satisfied with a chemical explanation alone, or with one at the biologic level only, or yet with one at the purely psychologic level—all three must give of their fraction in the total picture.

Apart from accident, much chronic so-called organic disease is a type of conservative response to such ideologic adaptations. In order to stay in the herd, one

may compromise his hostilities in some form of illness from which he resists being torn loose—"a behavior pattern has eaten its way into anatomical pattern and will not be recalled." "Why is it," Jelliffe asks, "that but about 1 to 2 per cent of the population have rheumatoid arthritis and yet 100 per cent of us harbor the specific parasitic enemies in the intestines, teeth, sinuses, [and] tonsils?" There are some pertinent studies to be made relative to the unconscious muscular tensions of love and hate, impatience and haste, grasping and greed and a host of other maladaptive tensions which express themselves in the muscle-tendon-joint trilogy. There is no doubt in the minds of the neuropsychiatrist that maladaptive tensions in these structures can and do modify the metabolism of the joints. They tend in no small measure to bring about changes which lock up the joints in arthritic bondage after months or years of faulty tensions.

Other problems of medicine have not been satisfactorily solved by internists, bacteriologists and immunologists: The tubercle bacillus is but one of the factors in this war of mycotic parasitism. Every man harbors the tubercle bacillus. The parasite is universal, but only a few succumb to it. It is not irrelevant to emphasize that the personality of the lung may be of more importance than the biochemical life of the parasite.

Flexor surfaces have a significance different from that of extensor surfaces, just as flexor muscles do different things than extensor muscles. The cutaneous areas of the former type are chiefly caressing goals; the latter, chiefly rebuffing. Ecology explains the location and type of lesion on the basis of cutaneous libido. Many young persons who present to the world repulsive facial acne are found on analysis to be punishing their faces with repulsive masks.

Heart disease is a fertile field for ecologic study. A tachycardiac compulsion neurosis is quite different from a tachycardiac conversion mechanism. There are a dozen tachycardias of different mechanistic origins which are often helped, even permanently relieved, by an enlightened psychotherapy. No one doubts the value of digitalis, quinine, morphine, rest or diet, but the "truth" is the only remedy for certain of these "emotional" cardiac disturbances.

The façade of urbanity is too often a disguise, a thin veneer for intense and strongly invested hostile cravings. "Nice people," "silk gloves" in manner and dress often are but marks for sadistic personalities. It is no wonder one finds high blood pressures and renal casts in the urine of many perfect "ladies" and "gentlemen."

All-around adaptation, in the medicine of the future, will occupy itself more and more with these "hostile impulses."

WISE, Howard, R. I.

THE RELATION OF PSYCHOSIS, MENTAL DEFECT AND PERSONALITY TYPES TO CRIME. WALTER BROMBERG and CHARLES B. THOMPSON, J. Crim. Law & Criminol. **28**:70 (May-June) 1937.

This is a report of all the cases which passed through the psychiatric clinic of the Court of General Sessions of the city of New York for a period of four years. It had previously been believed that criminals are largely psychopathic and feebleminded offenders. It was found, however, that the average percentage of feeblemindedness in this clinic was only 2.4 and that there were fewer feebleminded persons among the clinic prisoners than among drafted men in the army; the general tendency in the clinic criminals, however, was toward a lower mental age. Only 1.5 per cent were psychotic, and only 6.9 per cent were diagnosed as psychotic personalities. Of the 7,100 persons studied, 6.9 per cent suffered from some type of psychoneurosis. It was found that the aggressive antisocial type formed 7.3 per cent of the total group of "normal" criminals, the aggressive alcoholic type 0.4 per cent, the emotionally unstable type 11.3 per cent and the hysterical swindler type 1.4 per cent. The unethical group made up 2.5 per cent of the total; persons of the so-called shrewd and business man type, 1.7 per cent, and those of adolescent type, so called because of the immature makeup, 7.2 per cent. Immature adults constituted 3.1 per cent; egocentric persons, 5.3 per cent, and those of the shiftless, pleasure-loving, unhibited type, 8.4 per cent. Another large group (5.2 per cent)

was made up of suggestible or submissive criminals. The dull, adynamic type comprised 2.3 per cent; the nomadic type, 0.9 per cent; the primitive type, 1 per cent; the chronic alcoholic type, 2.5 per cent, and the organic unstable type, 0.4 per cent. Twenty-one per cent, or 1,490 patients, of the adjusted type probably would have been able to get along in the workaday world.

SELLING, Detroit.

THE USE OF THE BERNREUTER PERSONALITY INVENTORY AS AN AID IN THE PREDICTION OF BEHAVIOR PROBLEMS. GEORGE S. SPEER, J. Juvenile Delinquency **20**:2 (April) 1936.

As part of a general program of personality research, the Bernreuter personality inventory was given to all children in the ninth, tenth, eleventh and twelfth grades at the Mooseheart National Home and Training School. The results of tests on fifty-four problem children were compared with those of one hundred and eighty-five normal subjects. The author concludes: 1. The percentile rank on any of the four scales of the Bernreuter personality inventory, at least so far as this group is concerned, is of no value as an aid in prediction for problem children. 2. There is no significant difference in the scores of the problem group in any two of the four scales. 3. There is no significant difference between the scores of the problem and those of the nonproblem groups in any of the four scales. 4. The Bernreuter personality inventory is of no aid in prediction for problem children.

FERGUSON, Niagara Falls, N. Y.

THE REACTION OF CERTAIN PSYCHOTIC TYPES TO ALCOHOL. CARL E. TRAPP and PURCELL G. SCHUBE, J. Nerv. & Ment. Dis. **85**:668 (June) 1937.

Trapp and Schube report the effects of the oral administration of alcohol to psychotic patients, particularly with reference to any assistance which alcohol may lend in the study of the "intellectual, overt and emotional reactions." Twenty-one patients were studied; fifteen were suffering from dementia praecox, three from psychosis with mental deficiency and three from the depression of manic-depressive psychosis. Of the patients with dementia praecox, nine had the catatonic, four the paranoid, one the hebephrenic and one the simple type. The diagnosis in all cases had been established after prolonged study. Each patient was placed in bed, and a 40 per cent solution of alcohol was administered by nasal tube. The first dose was 30 cc., after which 15 cc. was given every four minutes, to a maximum of 120 cc. Subsequent doses of 15 cc. were then administered every ten minutes.

Fifteen of the twenty-one patients studied were mute; nine of these talked in varying degree during the experiment with alcohol. The emotional state of the patient with simple dementia praecox was unchanged, but the hebephrenia was elaborated in the one patient of this type. Of the nine patients with catatonic dementia praecox, five exhibited sorrow, sometimes altered by episodes of laughter; one showed erotic behavior, and three remained indifferent. The three patients with psychosis and mental deficiency exhibited marked depression and crying under the effect of alcohol, as did all three patients with manic-depressive psychosis. Negativism was not changed by alcohol. Temporary benefit was apparently achieved in six of the twenty-one patients. Trapp and Schube concluded from their own work that although therapeutic benefit of a temporary nature was obtained in certain cases, they could not verify the finding of Kantorovich and Constantinovich that permanent improvement or recovery can occur with one or two administrations of alcohol. They believe alcohol is of some value in the investigation of mental disease, chiefly by diminishing mutism and making patients more accessible for study. Alcohol also helps in the differentiation of catatonic and manic-depressive stupor, since the former is not altered by alcohol and the latter is changed by the elaboration of much depressing mental content, with its appropriate emotional content. Also, in patients whose psychosis conceals mental deficiency, the alcohol may lead to sufficient self-expression to reveal the underlying deficiency.

MACKAY, Chicago.

INTERMEDIATE METABOLISM OF THE BRAIN IN SCHIZOPHRENIA. TCHALISSOFF, N. M. WOLFSON and D. N. AROUTIOUNOFF, Encéphale **31**:174, 1936.

Blood was taken from the internal jugular vein, the brachial artery and the basilic vein in sixty cases of schizophrenia. This paper is a preliminary report on the results in thirteen cases. Normal subjects could not be obtained as controls. The amounts of potassium, iron and total phosphorus in the blood were found to be reduced. Calcium was present in normal amounts. The alkali reserve and the catalase were diminished in blood from the jugular vein. Residual nitrogen was retained in the brain in most cases. The brain discharged a great deal of uric acid, demonstrating the breakdown of nucleoproteins. Carbohydrate metabolism in the brain was increased. The level of dextrose in the efferent blood from the brain was raised, which is explained by an increased breakdown of glycogen in the brain. In keeping with this finding was the increased lactic acid content of blood from the jugular vein. Hexose phosphate (lactacidogen) was not involved in the cerebral metabolism.

LIBER, New York.

Meninges and Blood Vessels

STREPTOCOCCIC MENINGITIS AND ABSCESS OF THE BRAIN COMPLICATING SCARLET FEVER. M. B. GORDON, A. M. LITVAK and V. CARONNA, Am. J. Dis. Child. **53**:1447 (June) 1937.

Suppurative meningitis and abscess of the brain are rare complications of scarlet fever. The following types of meningeal irritation and meningitis may be observed in the course of this disease: (1) serous meningitis, probably a toxic reaction, in which the spinal fluid is increased in amount and pressure but is otherwise essentially normal; (2) lymphocytic meningitis, in which meningeal signs are more marked and the spinal fluid is clear and under pressure and contains a predominant number of lymphocytes but no bacteria; (3) sympathetic meningitis, a meningeal reaction to adjacent suppurative foci, in which there is polymorphonuclear leukocytosis but no bacteria are present in the spinal fluid, and (4) acute suppurative meningitis, characterized by turbid fluid containing many polymorphonuclear leukocytes and hemolytic streptococci. The complication last mentioned may occur without any demonstrable localized focus of infection and hence be "primary," or it may arise from a localized source and be "secondary."

Gordon and his associates report one case each of primary and secondary suppurative meningitis in which there was recovery; one of abscess of the right temporal lobe and sympathetic meningitis in which the outcome was fatal, and one of abscess of the left side of the cerebellum in which recovery followed drainage.

WAGGONER, Ann Arbor, Mich.

SPASM OF THE CENTRAL RETINAL ARTERY IN RAYNAUD'S DISEASE. R. G. ANDERSON and ELLIS B. GRAY, Arch. Ophth. **17**:662 (April) 1937.

Anderson and Gray state that ocular complications occur infrequently in Raynaud's disease and that spasm of the central artery of the retina is exceedingly rare. They report a case of Raynaud's disease in a man 39 years old in which angiospasm involved the central artery of the right eye. The patient improved under treatment with potassium iodide, but the retinal arteries on the right remained thin and bloodless. The disk showed definite pallor, and vision was reduced to the barest perception of light.

SPAETH, Philadelphia.

CEREBROSPINAL RHINORRHEA. DAVID H. BALLON and H. C. BALLON, Arch. Otolaryng. **25**:57 (Jan.) 1937.

Cerebrospinal rhinorrhea may be due to trauma or to new growth, or it may be spontaneous. The disease is one of youth and adult middle life. It is most

frequently unilateral. It may subside temporarily, but does not disappear. Optic findings, when present, are strikingly similar in all cases. One finds either optic neuritis passing into atrophy or typical postpapillitic atrophy. In five instances the visual fields were contracted. The visual outcome in five cases was bare perception of light or total blindness. In four instances the greater visual defect was noted in the eye on the same side as the nasal flow. Failure of vision preceded establishment of the flow in seven cases, the interval being from one to five years. On three occasions the flow began several years before the onset of ocular symptoms. The Ballons report the case of a man aged 53 who complained of right frontal headache, cough, cold in the head, insomnia and a feeling of weakness in the morning for two weeks, which were said to have followed exposure. An automobile accident two years before was followed by headache, which soon disappeared. One year before examination he had a clear, watery discharge from the nose, which ceased after four weeks. At the time of examination there was a constant drip of clear fluid from the right nostril; 12 cc. could be collected in ten minutes. The flow was faster when he leaned forward. The fluid generally tasted salty to him. It did not stiffen or stain the handkerchief. Roentgenograms of the sinuses were normal. The patient was kept awake at night by the nasal drip. Neurologic and physical examinations gave normal results, except that the pupils were small and reacted sluggishly to light and in accommodation. The diagnosis of cerebrospinal rhinorrhea was made on the basis of the discharge of clear fluid from the nose without visible local condition. The continuous discharge of cerebrospinal fluid accounted for the headache and fatigue. The Wassermann reaction of the blood was strongly positive, but that of the cerebrospinal fluid was negative. The protein, sugar, chlorides and sodium chloride contents of the cerebrospinal fluid were normal. After five months the discharge ceased and had not returned. This case illustrates the spontaneous type of rhinorrhea.

HUNTER, Philadelphia.

USE OF PARA-AMINO-BENZENE-SULPHONAMIDE OR ITS DERIVATIVES IN TREATMENT OF BETA HAEMOLYTIC STREPTOCOCCAL MENINGITIS. F. F. SCHWENTKER and others, Bull. Johns Hopkins Hosp. **60**:297 (April) 1937.

Schwentker and his collaborators used sulfanilamide or its derivatives in treatment of four patients with meningitis due to beta hemolytic streptococci. Two of the patients had a primary otitic focus and one a traumatic focus (craniotomy wound); in the fourth no purulent focus was discovered. In three patients surgical intervention (mastoidectomy or exploratory craniotomy) accompanied therapy with sulfanilamide or its derivatives. Three patients received intraspinal therapy with these chemicals, while for the other patient oral therapy alone was used. Three patients recovered, and one died. It appears that sulfanilamide or its derivatives offer the possibility of a specific chemotherapeutic approach to the treatment for beta-hemolytic streptococcic meningitis. A combination of oral and intraspinal therapy deserves a thorough trial. If the patient is not nauseated and can swallow, treatment should be started with sulfanilamide by mouth and by the intraspinal route. Tablets are used for oral administration. The total dose for the first twenty-four hours is calculated on the basis of three tablets (1 Gm.) for each 20 pounds (9 Kg.) of body weight, up to 100 pounds (45 Kg.). For adults with acute infections the authors believe that 5 Gm. of the substance represents the maximal daily dose.. This total amount is divided into four doses given at intervals of six hours. In preparing the drug for clinical use, it is their practice to dissolve 0.8 Gm. in 100 cc. of physiologic solution of sodium chloride which has been brought to the boiling point and then cooled to about 90 C. Such 0.8 per cent solutions of sulfanilamide may be used intrathecally. The general practice in administering the drug intrathecally should closely follow that recommended for the use of antimeningococcus serum in meningococcic meningitis; namely, rather complete spinal drainage by lumbar puncture should be instituted and then from 15 to 25 cc. of a warm, freshly prepared 0.8 per cent solution of sulfanilamide should be permitted

to flow in by gravity. If the patient cannot swallow tablets, treatment subcutaneously with prontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfuric acid) or an 0.8 per cent solution of sulfanilamide in sterile physiologic solution of sodium chloride may be instituted. With the former solution, 1 cc. per pound of body weight constitutes the total daily dose. This is divided into four equal doses given at intervals of six hours. If 0.8 per cent solution of sulfanilamide is used, it should be given by hypodermoclysis in the following amounts: for weights of up to 40 pounds (18 Kg.), 100 cc.; for weights of from 40 to 80 pounds (18 to 36 Kg.), 200 cc.; for weights of from 80 to 120 pounds (36 to 54 Kg.), 300 cc., and for weights of more than 120 pounds, 400 cc. in twenty-four hours. Therapy should be continued at the advised level until the spinal fluid has been rendered sterile for at least forty-eight hours and a marked general improvement in the patient's condition has occurred. At this point the intraspinal therapy may be discontinued and the amount of the drug given by mouth reduced by one-third. Adequate oral therapy should be maintained until the patient is entirely well. Surgical procedures designed to eradicate septic foci are indicated in streptococcic meningitis as an adjunct to specific therapy, but extensive surgical intervention should not be resorted to until the infection has been brought under control by specific therapy.

EDITOR'S ABSTRACT.

MENINGOCOCCEMIA WITHOUT MENINGITIS. F. W. GOUNDRY and T. H. PHALEN, New York State J. Med. **37**:491 (March 1) 1937.

Goundry and Phalen cite a case of meningococcemia unaccompanied by meningitis, in which the disturbance began with chills and fever and was accompanied by headache, pain in the joints and mental apathy. This was followed by profuse sweating and a generalized rash resembling the roseola of typhoid. The blood count showed moderate leukocytosis with a preponderance of polymorphonuclears. Meningococci were observed in the blood stream early in the attack. As the patient improved, the blood cultures became sterile. There appeared to be no indication for cultures of the petechiae and spinal fluid. The condition is proably more common than one realizes because facilities for blood cultures are not always at hand and enriched culture mediums must be used for isolation of the meningococcus. The physician is often unmindful of this disease and may easily overlook it, especially in the milder forms. The triad of chills, arthralgia and cutaneous eruption should prompt one to secure an early culture of the blood. From the therapeutic point of view, specific serum therapy is the treatment of choice.

EDITOR'S ABSTRACT.

RECOVERY FROM PNEUMOCOCCAL MENINGITIS. J. R. CALDWELL and P. S. BYRNE, Brit. M. J. **1**:1204 (June 12) 1937.

A girl aged 16 had sore throat, chills and headache. There were vomiting the next day and gradual loss of consciousness. The cerebrospinal fluid was under high pressure and contained 7,000 polymorphonuclear leukocytes and extracellular diplococci in great numbers. The precipitation test was positive for the type I pneumococcus and negative for the meningococcus. Delayed cultures were sterile. Treatment consisted of repeated spinal drainage and administration intramuscularly of the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonic acid and of the hydrochloride of 4-sulfamido-2′,4′-diaminoazobenzene by mouth. The patient was acutely ill for only three days and had completely recovered by the eleventh day.

ECHOLS, New Orleans.

BENIGN MENINGITIS OF SWINEHERDS. G. CHARLEUX, Presse méd. **45**:452 (March 24) 1937.

Acute benign meningitis, occurring mostly among fruit gatherers of Switzerland and Savoy, is known as benign meningitis of swineherds. It attracted attention recently

because from 5 to 10 per cent of the students of the dairy farms in Berne, Switzerland, fell victims to it. It was found to attack mainly young laborers who, besides gathering fruit, were occupied in the making of cheese, the by-products of which are fed to pigs. The pig is probably the transmitting agent. The intermediary host is not known. The disease begins suddenly with chills and high temperature, coated tongue, vomiting and obstipation or diarrhea. The feces have the odor of pigs. Violent headaches and dull sensorium have often led to the diagnosis of typhoid or paratyphoid. Both torticollis and Kernig's sign are marked. The patient is often restless but shows no somnolence or delirium. There is often lymphocytosis but no change in the number of mononuclears and polymorphonuclears. The disease is differentiated from tuberculous meningitis by the patient's state of good nutrition and the nature of his occupation. Furthermore, perspiration, cyanosis and slight eruption on the skin, added to the gastro-intestinal symptoms, facilitate the diagnosis. Lumbar puncture eases the headaches and seems to shorten the duration of illness. Phlebotomy also gives good results, probably by reducing the cerebrospinal tension. EDITOR'S ABSTRACT.

ENTEROCOCCIC MENINGITIS. B. KEMKES, Med. Klin. **33**:196 (Feb. 5) 1937.

After pointing out that meningitis of enterococcic origin is comparatively rare, Kemkes reports two cases that were recently observed at his clinic, in both of which the outcome was fatal. In the first case necropsy revealed purulent meningo-encephalitis, and in the second, purulent leptomeningitis. Bacteriologic examination in the first case disclosed enterococci in three specimens of cerebrospinal fluid and, during the necropsy, in two foci of pus in the brain; in the second case enterococci were observed in one specimen of cerebrospinal fluid and, during necropsy, in a focus of pus in the cerebellopontile angle. Tests with the various strains revealed enterococci of type B in both cases. Since the enterococci were present in pure culture in the spinal fluid as well as in the foci of pus, Kemkes thinks that doubtedly they caused the fatal meningitis.

EDITOR'S ABSTRACT.

VALUE OF DETERMINATION OF SUGAR CONTENT OF THE SPINAL FLUID IN DIAGNOSIS OF MENINGITIS AND COMMENTS ON POSTALIMENTARY HYPERGLYCORRHACHIA IN ACUTE INFECTIOUS DISEASES. N. I. NISSEN, Ugesk. f. læger **98**:1309 (Dec. 31) 1936.

Nissen found that after administration of large amounts of dextrose to patients with acute infectious diseases and meningitis postalimentary hyperglycorrhachia may be more marked than normal, but he emphasizes that no alimentary increase could be established after the intake of ordinary meals with slowly resorbable carbohydrate. On puncture the percentage of sugar was slightly higher in the first portion emptied than in the last, and in accord with this the suboccipital fluid in cases of tuberculous meningitis contained somewhat less than the lumbar fluid. The diagnostic value of sugar in the spinal fluid was tested for 529 patients, of whom part were normal and part had meningitis or meningeal irritation. Of 282 patients with benign disturbances of the meninges (acute anterior poliomyelitis, encephalitis or "meningitis serosa benigna"), only 3 showed values under 40 mg. per hundred cubic centimeters. Of 31 patients with malignant disorder of the meninges (tuberculous meningitis), 28 gave values under 40 mg. per hundred cubic centimeters. The boundary between benign and malignant meningitis is thus established at 40 mg. of sugar per hundred cubic centimeters. Normal values appear only in the earliest stages of tuberculous meningitis. Determination of the sugar in the spinal fluid is of even greater diagnostic value than cytologic examination and determination of the albumin content. EDITOR'S ABSTRACT.

Diseases of the Brain

LESIONS OF "ENCEPHALOMYELITIS" AND MULTIPLE SCLEROSIS: VENOUS THROMBOSIS AS THE PRIMARY ALTERATION. T. J. PUTNAM, J. A. M. A. **108**:1477 (May 1) 1937.

According to Putnam, the effects of venous obstruction in the central nervous system have been studied experimentally and pathologically. The two sets of observations lead to the same conclusions. The stasis affects the white matter more than the gray. The commonest lesion consists of swelling and disintegration of myelin upstream along the vein, accompanied in the severer lesions by some swelling and fragmentation of axis-cylinders. There is diffuse proliferation of astrocytes in the vicinity. At a later stage phagocytes containing products of parenchymal destruction accumulate within the adventitial sheaths of vessels. Occasionally cells resembling lymphocytes are seen. This histologic picture, characterized by the predominance of acute exudative phenomena, changes gradually to one in which cellular activity is almost at a standstill. At most, a few phagocytes are seen within hypertrophied adventitial meshes. The axis-cylinders resume a more normal appearance, and it often becomes difficult to be sure that any are missing. The destroyed myelin is apparently never regenerated, and the rough, indistinct edges of the area of myelin loss gradually become smooth and distinct. The glial fibrosis continues to grow more dense for at least a year after the insult has occurred. Many of the factors that may lead to diffuse thrombosis of small veins throughout the body correspond to the recognized antecedents of certain types of "encephalomyelitis" and the onset or exacerbation in some cases of multiple sclerosis. In both these groups of disease, thrombi and other evidences of vascular occlusion are observed in relation to the characteristic lesions and in other organs of the body. These lesions correspond closely to the experimental and spontaneous occlusion of veins. It is probable, therefore, that the primary alteration in certain types of "encephalomyelitis" and multiple sclerosis is an abnormal lability of the blood plasma, which may be caused to clot in venules of the brain (and other organs) by a variety of exogenous (and probably endogenous) factors.

EDITOR'S ABSTRACT.

CEREBRAL HEMORRHAGES FOLLOWING LUMBAR PUNCTURE. PURCELL SCHUBE and NAOMI RASKIN, J. Nerv. & Ment. Dis. **84**:636 (Dec.) 1936.

The reports in the literature of fourteen cases of cerebral hemorrhage following lumbar puncture were studied by Schube and Raskin. They believe that the lumbar puncture was a contributing factor in the intracranial and intracerebral bleeding and resulting death. The addition of a case of their own makes a total of fifteen. The number of deaths from cerebral hemorrhage, when compared with the frequency of lumbar puncture, indicates its rarity. In seven of the fifteen cases a tumor of the brain was the probable focus and cause of the bleeding. In two cases hemorrhage was caused by rupture of an aneurysm. There was no constancy in the place or position of the hemorrhage. In six cases the hemorrhage had ruptured through the wall of or into a lateral ventricle. There was no correlation between the quantity of fluid removed or the spinal fluid pressure and the hemorrhage. In seven cases the reaction occurred immediately after the puncture. There were no characteristic symptoms whereby the cerebral hemorrhage could be diagnosed other than those which accompany cerebral insult. The case reported by Schube and Raskin was one of neurosyphilis, accompanied by delusions of grandeur and euphoria. They state that the hemorrhage may have been due to increase in the blood pressure, weakness of the blood vessels resulting from syphilis or the use of arsenicals or both, decrease in the pressure outside the blood vessels or, last, a combination of the three preceding possibilities. It was evident that only a slight rise in blood pressure may have been necessary to produce the hemorrhage. What part stasis or resultant thrombi may play in promoting extravasation of blood into the surrounding tissues or in producing cortical rupture of the walls of the vessels is not yet established.

HART, New York.

THE ELECTRO-ENCEPHALOGRAM IN EPILEPSY. F. GOLLA, S. GRAHAM and W. GREY WALTER, J. Ment. Sc. **83**:137 (March) 1937.

In 91 of 214 cases of epilepsy in which electro-encephalograms were made there were abnormalities. Abnormal electro-encephalograms were characterized by the occurrence in any part of the cortex of waves with a frequency of less than 6 per second and of other waves resembling the alpha rhythm, but not originating in the parieto-occipital cortex and not affected by visual and mental activity. Minor epilepsy was usually associated with normal records, as contrasted with major epilepsy in which the records were usually abnormal. The more a condition tended to conform to so-called idiopathic epilepsy the greater was the incidence of abnormal electro-encephalograms. The higher the age of the patient the more likely was the record to be normal. In a few cases of organic epilepsy in which the electro-encephalogram was normal, it was found that convulsive seizures had occurred prior to the organic lesion. In a few cases of idiopathic epilepsy the records were normal; these occurred in old persons or in patients with hystero-epilepsy of purely psychogenic origin.

KASANIN, Chicago.

HEREDITY AND EPILEPSY: A STUDY IN TWINS. K. CONRAD, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:509 (June) 1936.

Conrad investigated the genetic factor in the etiology of epilepsy by studying discordant monozygotic twins one of whom had epilepsy. In a series which he observed personally and in two series reported on in the literature all the patients were mentally defective. Epileptic convulsions appeared late in life in only one of the twins, owing to an unknown exogenous factor. In eight series (three of which he observed personally) the epileptic attacks appeared in one of the twins after an infectious disease. The affected twin was usually backward. In one case encephalitis followed vaccination, and in others it was observed during the course of measles.

Conrad studied three pairs of twins one of whom became epileptic after a trauma to the head. Three similar instances are cited in the literature. In all but one of these cases epileptic attacks followed a cranial trauma before the tenth year. The appearance of the first attack in these cases occurred at varying periods after trauma. The clinical features were similar to those observed in genuine epilepsy in concordant twins, namely, onset of attacks between the ages of 4 and 13, absence of attacks early in the course and appearance of grand mal attacks later in the disease. These increase in frequency and are followed ultimately by mental deterioration.

This study of twins, one or both of whom had epilepsy, emphasizes the probable importance of the genetic factor in the etiology of this disease. Endogenous and exogenous factors cooperate to determine the appearance of convulsions in a given person at a particular time. Even when traumatic and other noxious agents operate such constitutional factors cannot be ignored. Idiopathic or genuine epilepsy and hereditary epilepsy must not be confused. Genuine epilepsy constitutes a large group of cases the etiology of which is not clear. Whether the anlage to epilepsy becomes clinically manifest depends on a complex constellation of internal and external factors. Conrad objects to the point of view of Marburg, who recently insisted that epilepsy is always due to exogenous causes.

SAVITSKY, New York.

CLINICAL ASPECTS OF MENINGIOMAS OF THE POSTERIOR FOSSA. I. RASDOLSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **156**:211 (Sept.) 1936.

From his series of 346 verified tumors of the brain, Rasdolsky reports 12 cases of meningioma in the posterior fossa. Twelve of the 62 meningiomas in the series were infratentorial and 50 supratentorial. Twelve of 110 infratentorial tumors were meningiomas. Two of the 12 tumors were on the right side, 9 on the left and 1 in the midline. All these meningiomas were extracerebral and intradural.

Three were of the flat type, of which 2 were in the cerebellopontile angle. In none of the cases was the nature of the tumor suspected before operation. The following clinical variants are described: 1. Basilar type (2 cases). The dominant feature in cases of this type is multiple pareses of the cranial nerves; involvement of the long tracts and increased intracranial pressure are not present. Signs of cerebellar involvement are usually also absent. The course is benign when only one side of the floor of the posterior fossa is involved. When the tumor is bilateral, the course is more rapid, probably owing to bilateral implication of the vagus nerve. The frequent localization of this type of neoplasm under the brain stem makes radical removal difficult.

2. Cisternal type (2 cases). Tumor of this type arises from the meninges in the region of the basilar cisterns and usually lies between the medial surfaces of the cerebellar hemispheres, over the vermis. The clinical picture is usually that of increased intracranial pressure. The cranial nerves are not involved.. The foramina of Luschka and Magendie are occluded. A tumor of this type can easily be pushed into the foramen magnum and may cause sudden death. It can be removed easily at operation. In both Rasdolsky's cases there was sudden death. The onset of illness is usually with attacks of occipital headache following inordinate physical effort. There may be an acute increase in intracranial pressure, with jamming of the brain stem and the tumor into the foramen magnum. Rasdolsky adds that in both his cases Bruns' sign was absent, which differentiates the condition from cysticercosis of the fourth ventricle. Absence of cerebellar signs differentiates it from cerebellar tumor, which occurs earlier in life. Ventriculography alone can distinguish it from a tumor of the third ventricle.

3. Meningiomas of the cerebellopontile angle (2 cases). Four per cent of the tumors of the angle in this series were meningiomas. If a tumor of this type grows anteriorly toward the acoustic meatus, the clinical picture may be indistinguishable from that of an acoustic neuroma. If it grows posteriorly and laterally, cerebellar signs may predominate. In both the cases reported the onset was with aural symptoms, and the course and clinical picture were identical with those of acoustic neuroma. Other cranial nerves may, however, be involved first, as in the case reported by Olivecrona in which progressive facial paralysis of the peripheral type was present for four years before the onset of a hearing defect. Roentgenographic changes in the region of the porus acusticus and the pyramid favor the diagnosis of acoustic neuroma.

4. Paramedian type (1 case). To this variant belong tumors in the midline, between the cerebellar hemispheres, or just lateral to the midline and superior to one of the hemispheres. These tumors may compress the quadrigeminal bodies, the cerebellar hemispheres or the pole of the occipital lobe. Compression of the occipital lobes takes place only when the tumor breaks through the tentorium. The clinical picture of these tumors varies considerably, depending on the structures compressed. The main complaints are occipital pains, followed by signs of involvement of the brain stem or a quadrigeminal syndrome. Signs of involvement of the cerebellum and cranial nerves are not usually prominent and appear later in the course of the disease. In the author's cases there was definite evidence of involvement of the quadrigeminal region. In all cases of atypical syndromes of tumor of the quadrigeminal plate exploration should be made and a paramedian meningioma of the posterior fossa excluded. The mildness of the cerebellar signs is probably due to the slow growth of the tumor and the well known capacity of the brain to adjust to the removal of and injury to cerebellar tissue.

5. Cerebellar type (3 cases). This is found in the lateral part of the posterior fossa. A tumor of this type compresses the cerebellar hemisphere. It usually arises from the walls of the lateral sinus.

6. Supracerebellar type (2 cases). Tumors of this type lie on the superior surface of the cerebellum, away from the midline. In addition to cerebellar signs, homonymous hemianopia sometimes occurs, owing to compression of the homo-

lateral occipital pole. Cerebellar signs appear late. The cranial nerves, especially the facial, are involved only in the later part of the disease. Involvement of the long tracts is unusual.

The early appearance and severity of occipital headache are emphasized in these cases. Local tenderness on percussion is more marked in cases of meningioma than in those of other tumors of the posterior fossa. A roentgenogram of the skull does not help as much as in the diagnosis of supratentorial tumor. Roentgenographic changes in the skull were observed in only 3 of 12 cases. In 2 instances the occipital bone at the site of the tumor was eroded, and in 1 there was increased vascularization in the region of the tumor.

Seven of the patients were men, and 5 were women. The predominance of men in all cases of meningioma has been noted by other investigators and is not a coincidence. Whether it is due to a difference in the structure of the meninges in men and in women or to the greater exposure of men to trauma is difficult to decide. The development of meningioma following trauma to the head has been reported by Frazier and Alpers, Spiller, Penfield and others. One of Rasdolsky's cases suggests the probable role of trauma.

The average age of these patients was 38.6 years, the youngest being 28. The course was usually shorter than that of supratentorial tumor; in 10 cases it did not exceed a year, and in several the duration was a few months. In only 1 case was pleocytosis observed. In this instance there was complication with arachnoiditis. The tumor itself, as well as the cerebellum, may slip into the foramen magnum. Ventricular puncture and drainage should be performed immediately in such cases.

The cisternal meningioma is most easily removed *in toto* and presents the least technical difficulties at operation. Meningiomas of the angle are often difficult to remove if they extend deeply and anteriorly. They are also known to bleed readily. Meningiomas of the floor of the posterior fossa which extend under the brain stem cannot as a rule be completely removed. The paramedian and laterally placed tumors may give trouble because of close connection with the venous sinuses and extensive and close union of the tumor with the dura mater. If the tumor grows into the bone, the latter should be removed. The operative results with meningioma are not as good as those with acoustic neuroma. Only 4 of 12 patients were operated on, 2 of whom died. The 2 patients who recovered had a tumor of the angle.

SAVITSKY, New York.

ENCEPHALITIS AND INFECTION. S. HERINGA, Nederl. tijdschr. v. geneesk. **81**:760 (Feb. 20) 1937.

Heringa reports the case of a youth aged 16 who, in the course of a septic infection originating in an injury to the left hand, suffered a cerebral disorder with the clinical aspects of lethargic encephalitis. Further, the author describes three cases of disseminated encephalomyelitis in which the influence of focal infection was evident. He assumes that preexisting neurotropic viruses were activated by the focal infection. Attention is called to the danger involved in dental intervention in neurotropic infections.

EDITOR'S ABSTRACT.

Peripheral and Cranial Nerves

EIGHTH NERVE HIGH TONE DEAFNESS FROM NUTRITIONAL STANDPOINT. G. SELFRIDGE, Ann. Otol. Rhin. & Laryng. **46**:93 (March) 1937.

Selfridge declares that the work of Peters, of Oxford, proves conclusively that some factor in the vitamin B complex is necessary for perfect biologic equilibrium. Thus, the oxidation-reduction system is necessary in order to prevent the accumulation of lactic acid in certain parts of the brain. The observation of definite demyelination in both branches of the eighth nerve in a series of rats and chicks placed on a diet deficient in the factors of the vitamin B complex, B_1B_2 and

especially the filtrate factors B_6B_7 or K_1K_2, as shown in Covell's histopathologic studies, warrants the assertion that lack of sufficient vitamin B in the human diet is the principal cause of the degeneration in the eighth nerve. The clinical use of B_1 parentally, B_1B_2 absorbate and particularly the rice bran B complex appears to be the cause of the improved hearing noted in the audiograms of clinical patients. Administration of large doses of carotene (30,000 units daily) over a period of months has caused no further change in hearing as demonstrated by the audiograms. Perhaps if the administration of carotene or vitamin A was carried on over a longer period, under control of the photometer, further changes might be noted. The use of thyroid, except possibly in rare cases, does not influence the changes in the nerve. Its effect probably is to help in the general metabolic processes. The lowered basal rate in many instances is related to nutritional deficiencies. The white edema observed by Cody in his animals kept on a diet deficient in vitamin B and seen in human beings with the pharyngoscope appears to be conclusive evidence of vitamin B deficiency. No interpretation can be made regarding the association of high tone deafness with the linear type of body build.

EDITOR'S ABSTRACT.

CERVICAL RIB AND SCALENUS ANTICUS SYNDROME. W. M. CRAIG and P. A. KNEPPER, Ann. Surg. **105**:556 (April) 1937.

In order to emphasize some points in the differential diagnosis of cervical rib and indications for and results of surgical intervention for the condition, Craig and Knepper report six cases. The clinical picture of cervical rib and that of the syndrome of the scalenus anticus muscle are similar, as are the indications for surgical removal and the operation. The symptoms result from compression or irritation of the brachial plexus and compression of the subclavian artery. Compression may be due to the presence of cervical rib, an abnormally low position of the shoulder, high fixation of the sternum and ribs, low origin of the brachial plexus or elevation of the first thoracic rib from spasm of the scalene muscles brought about by irritation of the brachial plexus. When cervical ribs cannot be demonstrated, resection of the scalenus anticus muscle is usually all that is necessary to relieve the symptoms. In the presence of a cervical rib without tendinous attachments or anterior obvious pressure from behind, resection of the scalenus anterior muscle is all that is necessary, but when there is evident pressure from the cervical rib or its tendinous attachment, resection of the rib and the attachment should be carried out. In carefully selected cases in which the symptoms point clearly to either presence of cervical rib or the syndrome of the scalenus anticus muscle, the result of surgical treatment is usually excellent.

EDITOR'S ABSTRACT.

FURTHER STUDIES ON THE EFFECT OF SECTION OF ONE PERONEAL NERVE OF THE ALBINO RAT ON THE INTACT NERVE OF THE OPPOSITE SIDE. KOZO TAMAKI, J. Comp. Neurol. **64**:437 (Oct.) 1936.

In a previous report Tamaki showed that after unilateral section of the peroneal nerve the number of myelinated fibers in the contralateral nerve failed to increase with age at the normal rate. The present study was undertaken to learn the effect of the operation on rats of different ages and the effect of variability in the length of the interval between operation and killing, as determined by the number of myelinated fibers and the cross-sectional area of the nerve. From comparison with the corresponding changes observed in nerves of litter mates used as controls during like intervals, Tamaki makes the following observations: 1. The normal increase in myelinated fibers is retarded. 2. In some cases there is loss of myelin sheaths. 3. There is retardation in the increase of the cross-sectional area of the nerve. The effects observed are attributed to the action of toxic substances arising from the sectioned neurons. FRASER, Philadelphia.

THE NOCIFENSOR SYSTEM OF NERVES AND ITS REACTIONS. THOMAS LEWIS, Brit. M. J. **1**:431 (Feb. 27); 491 (March 6) 1937.

Lewis states that the skin and mucous membranes of the body are supplied by a previously unsuspected system of nerves, to which he applies the term "nocifensor" because they are concerned with local defense against injury. These nerves are distinct from those conveying sensory impulses but, like the latter, are part of the posterior root system. The nocifensor nerves can produce local changes in the skin without intervention of the central nervous system, but it is possible that they are also capable of excitation from the brain or spinal cord. Lewis suggests that the nocifensor nerves cause the cellular elements of the skin to liberate potent substances into surrounding tissue spaces, thus controlling partly or wholly within the skin the important elements of defense, including inflammation. The action of the nocifensor system is, of course, explicable only on the basis of the "axon reflex."

The first observation leading to recognition of a nocifensor system of nerves concerns the spreading area of hyperalgesia which develops when the skin is injured locally. A tiny crush of the skin of the forearm causes an oval area of tenderness, from 5 to 20 cm. long, to develop within from ten to twenty minutes. It may last for several hours. The hyperalgesia is not referred from the brain or spinal cord. This can be demonstrated by anesthetizing a cutaneous nerve before pinching the skin. The crush is not felt, but the area of hyperesthesia appears as soon as the nerve recovers. That this hyperesthesia arises through a local nerve mechanism can be demonstrated further by making a small wheal with procaine hydrochloride before crushing the skin. In this case the hyperesthesia does not develop until the effect of the anesthetic has worn off. This also shows that the hyperalgesia is due not to diffusion of a pain-producing substance from the crushed skin but to the functional integrity of the cutaneous nerves. Moreover, the development of surrounding hyperalgesia as the area of crush recovers sensitivity demonstrates that the capacity to provoke distant hyperalgesia resides in and is maintained by the crushed skin; the products of injury, so to speak, act through the local nerve channels as soon as these are not blocked. The hyperalgesia is, of course, the ultimate result of reduction in the threshold for sensory nerves subserving pain.

Nerves for pain, touch, warmth and cold are not concerned with production of the altered tissue state underlying hyperalgesia, for the fibers of these nerves supply only a small area of skin. Sympathetic nerves play no part, for the phenomenon of spreading hyperalgesia occurs in a desympathectomized region.

Further proof for the existence of the nocifensor system is found in the fact that a similar area of hyperalgesia can be produced by stimulating electrically the trunk of a cutaneous nerve. If procaine hydrochloride is injected into the nerve and the stimulus is applied above the block the hyperesthesia does not develop, though the central nervous system receives the full sensory stimulus. If stimulation of the nerve is below the block it is painless, and when the nerve recovers the usual area of hyperalgesia is found.

A third argument concerns what Lewis calls the vascular flare surrounding a local injury. The flare is due to dilatation of small arterioles in the skin over an area of 5 cm. or more. That this flare depends on an intrinsic system of cutaneous nerves is shown by the fact that it can be provoked after all nerves to the skin have been divided and that it disappears after the sectioned nerves have had time to degenerate.

In summary, a certain type of cutaneous lesion causes the release of a product which sets the arborizing nocifensor system into action. The result is a change in the chemical reactions of the tissues over a wide area, including lowering the threshold for pain and resulting hyperesthesia. A different type of cutaneous lesion may cause other fibers of the nocifensor system to produce capillary dilatation or flush through the release of a substance resembling histamine. Causalgia is the result of irritation of nocifensor fibers in an injured nerve.

Lewis believes that the antidromic flush which results from stimulating the distal ends of sectioned posterior roots and the reaction of capillaries of the skin to prolonged cold may eventually be found to depend on the nocifensor system.

ECHOLS, New Orleans, La.

A NOCIFENSOR LESION OF THE HAND: A SYNDROME FOLLOWING TRAUMA AND ASSOCIATED WITH ADDUCTION OF THE SHOULDER. GEOFFREY J. LILLIE, Brit. M. J. **1**:1068 (May 22) 1937.

Lillie reports five cases of causalgia-like symptoms of the hand following injury above the wrist. Two of the patients had Colles' fracture; one, a fracture of the olecranon; one, a fracture of the clavicle, and one, traumatic arthritis of the shoulder. All were middle-aged women. In every case the arm had been immobilized in adduction. The symptoms common to all patients were pain in the shoulder and severe, constant burning pain in the hand and fingers, with increasing stiffness and extreme sensitiveness to both touch and changes in temperature. The skin of the hand and fingers was smooth and shiny. The color varied from red when warm to blue when cold. The interphalangeal joints were stiff and painful. In the older patients trophic changes were developing in the nails and fingers.

To explain these symptoms, Lillie refers to the nocifensor nervous system recently described by Thomas Lewis. He points out that immobilization of the upper extremity may result in a lax shoulder joint, especially in middle-aged women, and consequent stretching of the lowest trunk of the brachial plexus as it crosses the first rib. Stretching the nerve irritates the nocifensor fibers in that root. Such stimulation, according to Lewis, results in causalgia-like symptoms, such as flush and hyperalgesia, at the periphery.

By means of manipulation of the shoulder, heat and abduction splints Lillie benefited greatly all five patients.

ECHOLS, New Orleans, La.

ABOLITION OF THE PATELLAR AND ACHILLES REFLEXES WITH CONSERVATION OF OTHER TENDINOUS REFLEXES: DISTURBANCE OF MOTILITY OF THE IRIS (ADIE'S SYNDROME). FROGÉ and CHINIARA, Ann. d'ocul. **173**:823 (Oct.) 1936.

Frogé and Chiniara report a case of Adie's disease which they observed for one year. The condition was characterized by abolition of the achilles and patellar reflexes and of the light reflex in the right eye while the left reacted only to an intense stimulus. Anisocoria, with enlargement of the right pupil and variability in its diameter, was present. There was no family or personal history of syphilis, and the Wassermann and Vernes reactions of the blood were negative.

BERENS, New York.

SYNDROME OF POLYRADICULAR NEURITIS OF GUILLAIN AND BARRÉ OCCURRING IN A CHILD. J. ANSAY, J. belge de neurol. et de psychiat. **37**:311 (May) 1937.

Ansay reports a case of polyradicular neuritis with albuminocytologic dissociation in the cerebrospinal fluid which occurred in a child aged 8 years. The only residual signs were slight weakness of the muscles supplied by the peroneal nerves and a slight valgus deformity of each foot. Few cases of this syndrome occurring in children have been described; this is the fifth case in which typical findings are reported. The syndrome of Guillain and Barré is a definite entity, clinically and serologically; numerous cases have been observed in adults. The etiology of the condition is not known. Most authors believe that a toxic or toxic-infectious agent may produce the same picture.

WAGGONER, Ann Arbor, Mich.

GRAVE SYNDROME OF MYELORADICULAR NEURITIS IN COURSE OF TREATMENT WITH ATABRINE (AN ACRIDINE PREPARATION). P. VALENTINI, Pediatria **45**:51 (Jan. 6) 1937.

Valentini points out the toxicity of atabrine (an amino-acridine derivative) in the treatment for malaria in children and advises that small doses be used. A

case of acute cerebrospinal polyneuritis in a child who was given this drug is reported in the literature (Moschini). Valentini reports a case of grave myeloradicular neuritis in a child aged 5 years who suffered from malaria and was given a daily dose of 0.03 Gm. for five consecutive days. There developed a syndrome of grave flaccid paralysis of the muscles of the trunk and of the extremities, disturbances of respiration and hepatic function and vomiting. The immediate treatment consisted of hypodermoclysis and administration of stimulants and tonics, as well as belladonna for control of the vomiting. Later strychnine, epinephrine, iron and arsenic were given; diathermy was applied, and physical and respiratory exercises were performed by the patient. The grave symptoms ameliorated, but those produced by disturbances of the nervous system have remained stationary till the time of writing, for eighty days.

EDITOR'S ABSTRACT.

BRACHIALGIA STATICA PARESTHETICA: A VARIANT OF ACROPARESTHESIA. R. WARTENBURG, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:695 (Feb.) 1936.

Wartenburg describes a type of acroparesthesia found mainly in women between the ages of 40 and 60, and more rarely between 30 and 40. It is seen at times in men. Spondylitis of the cervical portion of the spine is often found. The usual picture is one of fleeting paresthesias on the ulnar side of the hand. Objectively, nothing is seen. The disturbances are most often noted in the morning, on awakening, and at night. At times the patients report a dull pain in the deltoid region for a few hours. The paresthesias sometimes extend up to the fifth but never below the eighth cervical segment. The patient may be awakened from sleep by the sensory distress. Sometimes a slight movement of the shoulder or limb may cause it to disappear. The dull pains on the outer side of the arm and the hypothenar eminence are not as readily affected. The care with which the bed is made is a factor. Changes in weather have little effect, though the complaints are more frequent during the winter. The inconstancy of appearance of the sensory disturbance is characteristic. Weeks may pass without any symptoms, and then for one or two days paresthesias on the ulnar side of the hand and pain in the deltoid region may appear. Numbness on the inner side of the hand may be severe and be accompanied by anesthesia, which may last only a few seconds. At times paresthesias (pressure, heat, tickling and "pins and needles") appear during the day in the hypothenar eminence. The left arm is more often affected than the right. In some atypical cases pain instead of the paresthesias may be present. These complaints may last for years, with spontaneous remissions. Motor pareses have not been observed. Foci of infection were not found in any of the patients. The sedimentation rate was normal in all. Vasomotor changes were absent.

Wartenburg is convinced that the paresthesias and pain are caused by depression of the shoulder girdle during sleep, producing pressure on the inferior part of the brachial plexus. Such depression of the shoulder is more frequent and marked in women and in asthenic persons. The brachial plexus as it passes over the first rib is particularly vulnerable to compression by surrounding structures, especially if they are displaced by a falling shoulder. The plexus is often caught between the first rib and the clavicle as the shoulder sinks. During sleep the muscles are relaxed, and the pressure on the plexus becomes continuous. The signs and symptoms in the upper cervical distribution are probably due to pull on the upper part of the plexus. The transitory involvement of the plexus is probably due to pressure on the vasa nervorum.

SAVITSKY, New York.

Treatment, Neurosurgery

TEN YEARS' EXPERIENCE WITH MALARIA IN NEUROSYPHILIS. UDO J. WILE and EUGENE A. HAND, Am. J. Syph., Gonor. & Ven. Dis. **20**:630 (Nov.) 1936.

During a ten year period Wile and Hand followed the careers of 354 neurosyphilitic patients who had had malarial therapy. Of these, 3.3 per cent died

during the course of the paroxysms. The pains of tabes and the confusion associated with dementia paralytica were often temporarily aggravated during the treatment, but in most instances spinal drainage effected relief. This suggests that acute edema was responsible for exacerbation of the disease. Of the patients with dementia paralytica, 53 per cent had remissions, to the extent of functioning with economic efficiency, and 29 per cent deteriorated or were not benefited. The others died. Of the tabetic patients 51 per cent were benefited, 44 per cent were made worse or were not helped and 5 per cent died. The results with juvenile dementia paralytica were more discouraging, as 70 per cent of patients were not helped, 24 per cent died and 6 per cent were benefited. Sixteen of the patients in the tabetic group had atrophy of the optic nerve, but in only five did the condition progress to complete blindness, as expected. In view of the failure of other types of therapy to check the advance of disease of the optic nerve, Wile and Hand are particularly encouraged by this result. The effects of malarial therapy on the spinal fluid were less striking; in only 13 per cent of cases was a previously positive Wassermann reaction converted into a negative one. In most cases, however, the spinal cell count was reduced to normal.

DAVIDSON, Newark, N. J.

PROLONGED SEDATIONS WITH SODIUM BARBITAL. PHILLIP POLATIN, Psychiatric Quart. **11**:213 (April) 1937.

The use of barbituric acid derivatives to produce narcosis or sedation, though ineffective in terms of ultimate psychiatric cure, is a means of improving the behavior of noisy or destructive patients. Polatin administered soluble barbital by mouth in an 8.5 per cent solution. The group of 100 patients to whom this was administered varied in age from 17 to 72; most were in the twenties. About half had schizophrenia; the rest suffered from mania, alcoholism, senility, neurosis or cerebral arteriosclerosis. Toxic symptoms did not occur, although in fully one fourth of the cases soluble barbital was given for twenty months. The initial dose was 1 fluidrachm (3.6 cc.), i. e., 5 grains (0.3 Gm.) three times a day, which was increased or decreased until a maintenance dose was reached. Of 100 patients, 20 were transferred to quiet wards, 7 were much improved (quiet, amenable and cooperative), 54 definitely improved (less irritable and more easily managed), 8 slightly improved and 11 not improved. Definite benefit, therefore, resulted in 82 per cent of cases. In no case, however, did prolonged improvement occur in the basic mental difficulty. Polatin suggests that soluble barbital is the drug of choice for control of disturbed behavior in psychotic patients.

DAVIDSON, Newark, N. J.

LUMINAL AND PROMINAL IN EPILEPSY: A COMPARATIVE STUDY. C. GUY MILLMAN, Brit. M. J. **2**:61 (July 10) 1937.

A comparison of the efficacy of medaral (n-methylethylphenylmalonylcarbamide) and phenobarbital was made by studying the records of all epileptic patients in a colony for mentally defective persons. Each patient had been observed during similar periods while taking the two drugs. In thirty-nine cases the total number of convulsions while the patient was taking medaral was found to be approximately one third of that during a similar period of phenobarbital therapy.

ECHOLS, New Orleans.

INTRASPINAL HORMONAL TREATMENT (EFFECT OF INTRASPINALLY ADMINISTERED INSULIN AND SOLUTION OF POSTERIOR PITUITARY IN CASES OF SCHIZOPHRENIA). A. STIEF, Monatschr. f. Psychiat. u. Neurol. **92**:346 (Feb.) 1936.

Fourteen patients with schizophrenia were treated with injections of insulin or of solution of posterior pituitary into the lumbar subarachnoid space. Insulin was given to ten patients in doses of from 10 to 40 units. Eight patients were given a single injection; one patient received two injections, and another, three. Single doses of from 0.5 to 1 cc. of solution of posterior pituitary were adminis-

tered to four patients. After treatment with insulin a satisfactory remission occurred in one case, and transitory improvement, in another. In almost all instances the treatments were associated with unfavorable effects, such as a rise in temperature of several days' duration, headache, dizziness, vomiting, bradycardia, loss of appetite and restlessness. One patient had a convulsive seizure, which was regarded as a manifestation of hypoglycemia. Numerous authors have shown that severe damage to the spinal cord may be caused by the subarachnoid injection of a variety of substances. Hence, this procedure cannot be advanced as a method of treatment unless the medicinal agent is greatly diluted; under such circumstances it is not possible, as a rule, to give doses large enough to be of value. The introduction of substances into the subarachnoid space for therapeutic purposes is indicated only in conditions such as meningitis, in which local effects are desired.

ROTHSCHILD, Foxborough, Mass.

THE INSULIN TREATMENT FOR SCHIZOPHRENIA. M. MÜLLER, Schweiz. Arch. f. Neurol. u. Psychiat. (supp.) **39**:9, 1937.

Müller presents a statistical survey of the results obtained with the insulin treatment in 495 cases of schizophrenia in twenty-two Swiss institutions. He expresses the view that these statistics should be reliable, since methods of treatment and criteria both for diagnosis and for evaluation of results were fairly uniform throughout the various institutions. Social or complete remissions were reported in 59.1 per cent of 210 cases in which the duration of illness was six months or less, and in 57.2 per cent of 283 cases in which it was a year or less. In 88 cases in which the duration of the disease was from one to two years the percentage of good remissions fell to 27.3. In all cases in which the outcome was favorable, the average length of treatment was forty days in those in which the duration of illness was six months or less, and sixty days in those in which it was longer. This result indicates the necessity for more prolonged treatment in the latter group. Müller expresses the view that injections of insulin must be given for sixty days in order to determine whether the treatment will be of value and, further, that treatment should be continued for ninety days before being abandoned. By elimination of the cases in which the results were poor and treatment was not given for a sufficiently long period, the percentage of good remissions was raised to 64.3 in cases in which the duration of the illness was a year or less; by elimination also of cases in which treatment was insufficient but some improvement was shown, the percentage was raised to 71.1. Good remissions were obtained in 57.7 per cent of 206 cases of schizophrenia in which there had been one attack and in 51.9 per cent of 77 cases in which there had been previous attacks. Even multiple recurrences did not seem to alter materially the prospects for benefit. Of all cases in which social or complete remissions were obtained as a result of treatment, in some of which remission had persisted for as long as eighteen months, recurrences were reported in 6.4 per cent; relapses occurred in 8 per cent of 17 cases in which there merely was some improvement.

With regard to the cases in which the duration of the disease was a year or less, good remissions were reported in 64 per cent of 64 cases of the paranoid form of schizophrenia, in 63.3 per cent of 101 cases of catatonic excitement, in 55.5 per cent of 63 cases of catatonic stupor and in 48 per cent of 99 cases either of hebephrenia or of a form of schizophrenia not otherwise classified. Of cases, on the other hand, in which the duration had been more than a year, the percentage of good remissions in the paranoid group (13.8) was even lower than that in the hebephrenic group.

Only 2 deaths occurred in the 495 cases in which insulin treatment was instituted, in 1 of which the relation of treatment to the fatal outcome was questionable. Though Müller is opposed to too rigid standardization of procedure, he believes that departures from the standard technic should be attempted only by those who have had long and intensive experience. He adheres in general to the rules for treatment formulated by Frostig.

Müller mentions in passing many of the problems, as yet unsolved, which have arisen since the introduction of the new treatment. The fact that the patient with typical schizophrenia is the most favorable subject for insulin therapy and that the patient with manic-depressive psychosis or schizophrenia with manic-depressive features generally does poorly suggests that the effect of insulin is specific for schizophrenia. There is no general agreement, on the other hand, as to what is typically schizophrenic, nor does the concept of schizophrenia seem to represent a biologic unity. Unfavorable as well as favorable results, furthermore, will be obtained with insulin therapy in any form of schizophrenia, regardless of how one may classify the patients. It is difficult, therefore, to believe that the effect of insulin is specific. In spite of the fragmentary nature of knowledge in regard to the action of insulin and the vast amount of work yet to be done, Müller believes that the insulin treatment has stood well its first test.

DANIELS, Denver.

RESULTS OF CONVULSION THERAPY AT THE PSYCHIATRIC CLINIC, BERNE, SWITZERLAND. O. BRINER, Schweiz. Arch. f. Neurol. u. Psychiat. (supp.) **39**:118, 1937.

Results of treatment with convulsions induced by intravenous injections of metrazol in 111 cases of schizophrenia are reported. The duration of the disease was more than five years in 54 of the cases; in many instances the acute form had proved resistive to other forms of treatment. Briner regards the metrazol treatment merely as one of the means whereby contact with the patient may be established, thus rendering him accessible to psychotherapy. Of 34 patients who had had symptoms for less than a year, 50 per cent made a social recovery, 9 per cent were discharged in an improved condition and 24 per cent benefited from treatment but remained in the hospital. Although social recoveries were much less frequent when the disease was of long duration, institutional improvement was achieved in more than half the cases. The best results were obtained in patients with catatonic states, particularly those coming on later in life, with depression and hypochondriacal ideas; all 8 patients in the latter group recovered completely after a few injections. Mute, negativistic catatonic patients, on the other hand, did poorly, but mildly stuporous persons responded well. No great improvement was seen in paranoid patients with more or less systematized delusions of long standing, as compared with others with many hypochondriacal complaints and somatic hallucinations, who reacted favorably.

Two patients died during treatment; one had a goiter causing tracheal compression, and the other, who had unsuspected pelvic thrombophlebitis, succumbed to pulmonary embolism. The few recurrences noted were attributed to the fact that additional injections of metrazol were not given after a remission had been obtained. In conclusion, Briner states that one who has seen patients previously in need of constant care regain the zest for living and return to work can no longer doubt the value of the new treatment.

DANIELS, Denver.

RATIONAL ROENTGENOTHERAPY OF ACUTE NONSUPPURATING INFLAMMATIONS OF THE SPINAL CORD. P. DEL BUONO, Strahlentherapie **58**:251 (Feb. 17) 1937.

Del Buono discusses roentgenotherapy for acute anterior poliomyelitis in children, acute and chronic poliomyelitis in adults and acute and chronic multiple sclerosis. He reaches the conclusion that roentgenotherapy is advisable for nonsuppurating, acute inflammatory disorders of the spinal cord because it produces better results than other methods. The best results are obtained with acute anterior poliomyelitis in children, provided the treatment is begun early, that is, before the anatomic lesions of the spinal cord have become extensive. Favorable and lasting effects can be produced also in adults with anterior poliomyelitis, acute multiple sclerosis or radiculomyelitis, but in these conditions, also, early beginning of the treatment is essential. In chronic multiple sclerosis the effect of roentgenotherapy is slight. The improvement that may be noticeable after the first series of irradiations is not lasting, and after it disappears the disease process advances

unchecked. The technic of irradiation is of minor importance, for favorable results have been obtained with various methods.

EDITOR'S ABSTRACT.

INFLUENCE OF MALARIAL THERAPY ON THE HISTOPATHOLOGIC PROCESS IN THE SKIN ASSOCIATED WITH PROGRESSIVE MUSCULAR DYSTROPHY. A. ROTTMANN, Wien. klin. Wchnschr. **50**:1037 (July 9) 1937.

After review of a previous report on malarial therapy for progressive muscular dystrophy in which he demonstrated that at the onset and during progressive exacerbations of the dystrophy malarial therapy promises favorable results and that in late stages it may arrest the disease process and induce a favorable general condition, Rottmann describes his studies on the histologic changes produced by the therapy. He says that it was tried in cases of muscular dystrophy because of its activating effect on the defense powers of the organism. He reports on histologic studies in three cases, representing three stages. The histologic studies on the skin were made before and after the therapy. They reveal anatomic regression of the chronic infiltrative process and are further proof that malarial vaccination exerts a specific action on the tissues.

EDITOR'S ABSTRACT. [J. A. M. A.]

RESULTS OF INSULIN SHOCK THERAPY FOR SCHIZOPHRENIA. M. MARZYŃSKI and ST. WITEK, Ztschr. f. d. ges. Neurol. u. Psychiat. **159**:704 (Sept.) 1937.

Marzyński and St. Witek report the results of insulin shock therapy in 164 cases of schizophrenia in a hospital in Wilno, Poland, between February 1934 and October 1937. Intramuscular injections of insulin were given, beginning with 20 units and increasing gradually to the point of shock. The amount of insulin needed to produce shock varied from 24 to 368 units. At first only from twelve to fifteen severe shocks were given; this number was later increased, especially in cases of paranoid schizophrenia. The duration of the treatment did not exceed ninety days. The injections were usually given every second day. Patients were usually left in shock for two or three hours, but never more than five hours. Shock was prolonged in cases of paranoid dementia praecox. There was no death in this series. The authors excluded from the series cases (37) in which a tendency to spontaneous remission had previously been shown. They summarize their results in 127 cases as follows: Of 43 cases in which the duration of the disease was from one to six months, there was either recovery or marked improvement on discharge in 55.8 per cent. In 6 of these cases there was recurrence of symptoms later, the percentage of persistent recoveries being thus reduced to 41.8. Of 27 cases in which the duration was from seven to twelve months, there was recovery or great improvement on discharge in 14.8 per cent. In 2 cases marked improvement was shown later, which increased the percentage to 29.6. Of 57 cases in which the duration of illness was over one year, there was recovery or marked improvement in 5.2 per cent.

The authors emphasize that the best results with this treatment have been observed in cases in which the illness was less than six months. In the majority of cases improvement is seen after three or four weeks, occasionally after the first few shocks. They point out the high incidence of spontaneous remissions in this series (37 of 164 cases) and warn that this fact must be borne in mind in evaluating the ultimate results of the insulin treatment.

SAVITSKY, New York.

TREATMENT OF ACUTE CHOREA WITH BLOCK OF THE SYMPATHETIC NERVOUS SYSTEM. D. M. ZALKAN and E. M. EBICH, Vrach. delo **20**:114, 1937.

Zalkan and Ebich report fifteen cases of acute chorea in which treatment consisted of block of the sympathetic trunk with procaine hydrochloride. Therapy was successful in thirteen cases; the earlier it was begun the more striking was the result. The effect of block in the early stages was rapid, and in some cases, abortive. Prompt improvement in the symptoms frequently took place on the day

following the injection, all symptoms disappearing in the course of the next four or five days. Decisive improvement was likewise noted in patients with disease of longer duration, but the recovery consumed more time—from ten to fifteen days. These patients were given two or three additional injections. The treatment failed with two patients, aged 25 and 15 years, respectively, who had had a long illness —one for one year and one for six months. Good results were obtained in treatment for recurrences as well as for disease of recent origin. There were no recurrences in patients who had been cured. The authors experienced no difficulty in applying the method to treatment for children. The procedure consists of injecting into the region of the renal fossa from 60 to 100 cc. of a 0.25 per cent solution of procaine hydrochloride on the side of the predominating symptoms. From one to three injections were given. EDITOR'S ABSTRACT. [J. A. M. A.]

Special Senses

ETIOLOGY OF FAMILIAL DISEASES OF THE OPTIC NERVE. A. RIFAT, Ann. d'ocul. **173**:702 (Sept.) 1936.

Familiar diseases of the optic nerve occur in three forms: 1. Leber's subacute retrobulbar neuritis. The lesions involve only the macular fibers of the optic nerve. The disease progresses for about a year and then remains stationary; it does not result in total blindness. It occurs most frequently between the ages of 20 and 30 years. 2. Familial and complete atrophy of the optic nerve. Atrophy of all the nerve fibers results. Absence of central scotoma and peripheral contraction of the visual field differentiate it from Leber's disease. Partial blindness is usually present; complete amaurosis rarely occurs. In both the subacute retrobulbar neuritis of Leber and familial and complete atrophy of the optic nerve the etiology is unknown. 3. Familial and congenital atrophy of the optic nerve. The condition is present at birth and occurs in numerous members of the same family in the same generation and in successive generations. Heredity is direct or collateral.

Leredde expressed the belief that heredosyphilis is a causative factor in Leber's disease, in familial atrophy of the optic nerve and in the associated motor and intellectual syndromes. Syphilis must be searched for systematically by all available means and in all cases of familial disease of the eye.

BERENS, New York.

CHEMICAL CONSTITUENTS OF THE RETINA: THEIR RELATION TO VISUAL PURPLE AND THE THEORY OF DUALITY OF VISION. M. L. VERRIER and M. R. PANNIER, Ann. d'ocul. **173**:824 (Oct.) 1936.

Verrier and Pannier studied the chemical composition of the retina in twenty species of animals (mollusks, fish, reptiles, birds and mammals). They drew the following conclusions: Vitamin A and albuminous carotenes are present in all retinas. Only the albuminous carotenes appear to differ qualitatively and quantitatively in scotopic and in photopic retinas. Vitamin A presents no variation in structure in the different retinas. It is not a sensitizer of the visual cells. The retina contains the same chemical constituents in all classes of animals studied; variations in structure depend on the relative amounts of these constituents. The findings of Verrier and Pannier confirm the morphologic observations and uphold the unicist theory of single binocular vision.

BERENS, New York.

DOES ERGOTAMINE TARTRATE PARALYZE THE SYMPATHETIC NERVE TO THE IRIS? E. FROMMEL and D. ZIMMET, Ann. d'ocul. **174**:178 (March) 1937.

Frommel and Zimmet conclude from their experiments on rabbits that miosis caused by ergotamine tartrate (gynergen) is not of the paralytic type, for excita-

tion of the sympathetic fibers still produces mydriasis. Ergotamine tartrate does not, therefore, completely paralyze the sympathetic nerve of the eye. Moreover, ergotamine tartrate does not affect the action of epinephrine on the sphincter iridis. This conclusion conforms with knowledge concerning the influence of ergotamine tartrate on the tonicity of certain muscles (those of the pylorus, uterus and arterial coats) and the action of various compounds of ergot.

BERENS, New York.

IMMEDIATE BLINDNESS AFTER VIOLENT CRANIAL TRAUMA. JEAN SÉDAN, Rev. d'oto-neuro-opht. **15**:96 (Feb.) 1937.

The case was that of a man who fell down an elevator shaft, striking his head. After a short period of unconsciousness he complained of complete blindness, violent headache and a pulsating sensation in the right temporal region. Examination of the eyegrounds, forty-five minutes after the accident, revealed abundant hemorrhages in each retina, almost identical in size and position in the two eyes and confined to the temporal sides. The pupils were dilated, and the light reflex was completely abolished. Death occurred within a few hours. Autopsy revealed a temporoparietal fracture and a large extradural hematoma. The pressure of the clot was most marked in the region of the rolandic fissure, but no macroscopic evidence of injury of the brain was observed. Particular attention was directed to the occipital lobes and the optic nerves, but no lesion, macroscopic or microscopic, was discovered. The retinal hemorrhages could not account for the complete and instant blindness, accompanied by areflexia and mydriasis. Sédan believes that the blindness was the result of an intense, post-traumatic cortical angiospasm. In cases of cortical blindness the photomotor reflex is usually preserved, although Josserand and Pauly observed a case in which it was abolished. The mydriasis may be explained by the traumatism and ecchymoses of the face.

DENNIS, San Diego, Calif.

NYSTAGMUS PROVOKED IN THE COMATOSE STATE. I. ALFANDARY, Rev. d'oto-neuro-opht. **15**:161 (March) 1937.

Stimulation of the vestibular apparatus during states of coma has generally been thought to result only in abolition of the quick phase of nystagmus, the eyes being drawn in the direction of the slow component. Alfandary studied the vestibular reactions to caloric stimulation of eleven patients in coma, chiefly of apoplectic origin. The results were: (1) loss of the quick component of nystagmus, (2) disturbance of equilibrium between the two phases, so that the rapid phase occurred only at the beginning or the end of the test or persisted with the eyes in the deviated position and (3) slow deviation of the homolateral eye. A possible explanation of these phenomena is that the rapid phase, being the more recent phylogenetically, disappears first; then follows disappearance of associated movements and, finally, of all movements. These three modalities of the response to caloric stimulation do not represent three phases in the evolution of the comatose state. The only constant sign that accompanies progression of the comatose state is elevation of the threshold of excitation. Clinical and experimental researches indicate that the centers for both the slow and the rapid phase of nystagmus are located in the cerebrum, but in different places.

DENNIS, San Diego, Calif.

HYSTERICAL DEAFNESS. G. BUZOIANU, Rev. d'oto-neuro-opht. **15**:174 (March) 1937.

Hysterical deafness, especially the unilateral pure form, is rare. Two types are distinguished: pure hysterical deafness and hysterotraumatic deafness. The deafness may be total or partial and may involve one or both ears. It may be

isolated or accompanied by paralysis of other cranial nerves, by hemianesthesia of the skin or mucous membranes or by other disturbances of function. The duration of the disease may be a few days or several years, and recovery may occur spontaneously, as the result of an unexpected suggestion. Cases of unilateral deafness offer great diagnostic difficulties because the preservation of the cochlear reflexes usually observed in cases of bilateral deafness is of no value if hearing is retained in one ear. A valuable diagnostic sign is the absence of a "false Rinne reaction," which is always present in cases of unilateral deafness of organic origin. The case of a young woman with total unilateral hysterical deafness is reported in detail. The nature of the trouble was recognized by the absence of the false Rinne reaction; immediate recovery was obtained by use of suggestion. In the beginning of the illness, all the hearing tests gave no response; after recovery they were normal. A number of cases of hysterotraumatic deafness occurred during the World War, as a result of the effect of exploding projectiles. Patients with this type of deafness should be referred to a psychotherapeutist.

DENNIS, San Diego, Calif.

VESTIBULAR DISTURBANCES OF CENTRAL ORIGIN: CROSSED AREFLEXIA AND TYPICAL VESTIBULAR DISHARMONY. J. A. BARRÉ and J. P. KIRCHER, Rev. d'oto-neuro-opht. **15**:241 (April) 1937.

Barré and Kircher suggest the term *hémiavestibulie latérale homonyme* to designate their syndrome of vestibular disharmony. A man aged 43 was wounded in the left occipital region during the World War. Headaches and disturbance in equilibrium soon appeared and increased in severity during the succeeding years. Examination revealed diplopia, disturbance of associated movements of the eyes, limitation of ocular movement to the left and nystagmus to the left. There was deviation of the extended arms to the left. Caloric tests with water of 27 and 44 C. gave correct reactions, but the threshold varied. In the right ear reaction occurred with the use of 40 cc. of cold water; with warm water the threshold was obtained only after the use of 200 cc. In the left ear the thresholds were 100 and 40 cc., respectively. The threshold with the galvanic current was at 1.2 milliamperes in the right ear and at 3 milliamperes in the left. A few signs of cerebellar disturbance were elicited, more marked on the left side. The patient's condition improved, and he returned home. He was admitted to the hospital three years later, complaining of severe headaches, change in disposition, vertigo, diplopia, intermittent vomiting and stiffness of the neck. Cerebellar tests gave slightly incorrect reactions on the left side. Spontaneous nystagmus and deviation of the left arm to the left were present. The threshold of reaction to cold water was obtained with 125 cc. in the left ear and with 300 cc. in the right ear. The headaches grew worse, and paresis of the palate, vomiting, bradycardia and slow respiration followed. The eyegrounds were normal. Exploration of the posterior fossa revealed three small, encapsulated abscesses and a deeper, larger abscess with thin walls in the cerebellum. After recovery from operation the clinical vestibular signs were nystagmus, deviation of the left arm to the left and falling to the right in the Romberg test. In the caloric tests there was marked inequality of the threshold for warm and cold water and for the two ears. There were hyperreflexia of the vestibular fibers which cause nystagmus to the left and hyporeflexia of those which cause nystagmus to the right. This case demonstrates that it is possible to isolate two groups of vestibular symptoms, each with its own cause and evolution. The subjective symptoms of hypertension disappeared after the operation, and the signs of damage to the vestibular system persisted. The original injury caused, first, damage to the vestibular and cerebellar pathways in the brain, probably from small hemorrhages, and, second, a group of late disturbances, attributable to a minimal, but persistent, infection, culminating in formation of abscesses.

DENNIS, San Diego, Calif.

CHOKED DISK. ROBERT BING, Schweiz. Arch. f. Neurol. u. Psychiat. **39**:49, 1937.

The so-called transport theory of choked disk has found general acceptance. Even those who attach significance to compression of the ophthalmic vein regard this as secondary in importance to hydrops of the intravaginal space of the optic nerve. According to this theory in the syndrome described by Foster Kennedy, early compression of the optic nerve on the side of the tumor tends to prevent cerebrospinal fluid from being forced into the sheath of the corresponding nerve and this interferes with development of edema of the disk on that side.

The presence of choked disk is indicative of a space-taking process within the cranium, despite the fact that this sign has been encountered in certain conditions in which an expanding process would not a priori be expected. In this connection, Bing discusses the confusion of the terms "papilledema" and "optic neuritis" and the means of differentiating the two conditions. He admits the possibility of occurrence of true papilledema in the course of multiple sclerosis and expresses the view that in this condition, as well as in the various forms of encephalitis, edema of the optic disks is due to transient hydrops of the ventricles or to circumscribed serous meningitis. That the papilledema observed in association with leukemia and certain anemias is due to toxic edema of the brain or to hypersecretion of fluid appears more than probable. A similar cause is generally assumed for the papilledema seen in cases of nephritis.

The frequency of tumor of the brain in cases of papilledema ranges, according to published statistics, from 59 to 90 per cent; in Bing's opinion, a frequency of 75 per cent is too low rather than too high. Statistics on the varying frequency of choked disk in association with tumors of different locations in the brain have two principal sources of error: (1) the failure to give proper consideration to the stage of the disease at which the eyes were examined, and (2) the relative infrequency of thorough postmortem study. It is well established that tumors in the roof of the fourth ventricle or in the region of the aqueduct of Sylvius are especially apt to cause marked choking of the disks. It is also established that dilatation of the ventricles may follow occlusion of the foramina of Monro, Luschka or Magendie. It is believed that closure of the foramina in the posterior fossa is especially likely to occur when a growth in any location forces the cerebellar tonsils into the foramen magnum, although obliteration of the subarachnoid space by swelling of the parenchymatous elements may alone prevent the normal escape of fluid from this region. Choked disk is infrequent in association with basilar tumors of the middle fossa. Bing mentions hypersecretion of spinal fluid and cerebral edema resulting from venous stasis as causes of choked disk in order to serve as a warning against the assumption of a single mechanism for the production of choked disk by tumor of the brain. DANIELS, Denver.

Diagnostic Methods

THE MORO REFLEX. M. B. MCGRAW, Am. J. Dis. Child. **54**:240 (Aug.) 1937.

McGraw studied the Moro or body-startle response in fifty-seven infants. This reflex was elicited by suddenly striking the mattress on which the infant was lying, about 6 inches (15 cm.) above the top of the head. There was sequential change in the response as the child grew older. The first phase was usually present until the infant was 90 days old and consisted in bilateral extension and abduction of the upper extremities, ending in bowing of the arms over the thorax, extension and fanning of the digits except for flexion of the distal phalanges of the index finger and thumb, and extension of the spine and legs. The second or transitional stage occurred usually between the age of 90 and 130 days. Here, the grosser movements were diminished; the child merely extended and abducted the upper extremities, jerked the knees and cried less intensely. At the age of 210 days the child had passed into the mature phase. Overt somatic activity was practically suppressed, the characteristic reaction being merely a fine body jerk associated with blinking.

The mechanism of the reflex may be explained essentially as follows: In the first phase the cortex is not functioning; hence the subcortical nuclei are in charge of the somatic musculature. Since definite pathways are not established, there is flooding of the motor segments caudal to the midbrain with nerve energy which expends its force on motor agents through the intersegmental association fibers and sets off a diffuse defensive extensor reaction. During the second phase myelination takes place, and the neural pathways become more closely linked, which accounts for the reduction in somatic response. By the time the mature phase has developed the cortex is engaged, so that before the complete reflex can take place cortical inquiry into the meaning of the startle is activated. Further somatic activity depends on cortical deliberation. Since the Moro reflex is a behavior pattern, it may be useful in studying the development of other types of behavior.

WAGGONER, Ann Arbor, Mich.

EXTENSION OF THE THUMB: A NEW PYRAMIDAL REFLEX. W. A. BACHTIAROW, Schweiz. Arch. f. Neurol. u. Psychiat. **39**:45, 1937.

Acting on the thought that the various means of eliciting pathologic reflexes in the lower extremity should be applied to the upper extremity, Bachtiarow discovered a type of response which, so far as he knows, has not been described previously. In eliciting this new reflex, which is analogous to Oppenheim's reflex in the leg, the examiner lightly grasps the patient's hand, which must be relaxed, while with the thumb and index finger of his other hand, using light pressure, he strokes the radius in a downward direction. Normally flexion of the terminal phalanx of the thumb follows this maneuver, whereas in cases of disease of the pyramidal tract there is usually extension of the thumb. In some cases the response is limited to slight abduction. The sign is regularly elicited in hemiplegias of recent origin but may not be obtained in old hemiplegias because of the marked contracture.

DANIELS, Denver.

NEWLY DISCOVERED CEREBROPATHOLOGIC PHENOMENON. J. GERSTMANN, Wien. klin. Wchnschr. **50**:294 (March 5) 1937.

Gerstmann describes a cerebral phenomenon that he observed in a woman aged 33. The patient had headaches in the right upper parietal region, which area was also sensitive to pressure and percussion. Occasionally there were jacksonian attacks involving the contralateral (left) side of the body. These and other symptoms, as well as the encephalographic observations and the course of the disease, indicate a pathologic process in the retrocentral region of the cortex of the right cerebral hemisphere, chiefly the right upper parietal region. The extremely slow course suggests a benign tumor. The phenomenon to which Gerstmann calls attention is elicited as follows: If black or colored glasses that are impervious to light are placed before the patient's open eyes and he is told to look without directing the eyes in any other direction, there develop rhythmic automatic movements in the anteroposterior direction. These movements cannot be voluntarily altered or suppressed by the patient. If he is standing they involve the entire body; if he is sitting, only the trunk and head, and if the trunk is fixed, only the head. As soon as the patient closes his eyes the movements cease, but, if he opens them again behind the impervious glasses the movements reappear. The patient experiences the movements in the anterior direction as a forward traction that cannot be resisted; the backward movements he is unable to explain. Passive turning of the head in the direction contralateral to the cerebral focus intensifies the rhythmic oscillating movements, and the patient utters an anxious cry in response to the intense sensation of falling toward the left. Passive movement of the head in the direction homolateral to the focus (that is, toward the right side) does not intensify the movements. Passive forward bending of the head and fixation in this position likewise intensify the rhythmic anteroposterior movements. Active movements of the head have similar effects. The body move-

ments are accompanied by ocular movements, but the latter take the opposite direction. Further studies proved that the movements can be elicited by placing before the eyes any uniformly colored (except white or gray) surface. However, as soon as fixation is effected by a definite outline, or even by the prick of a pin in the otherwise uniform surface, the rhythmic body movements cease. Thus, the movement phenomenon is elicited only if the eyes are open and fixation is impossible. This phenomenon gives rise to a number of questions that remain unexplained.

EDITOR'S ABSTRACT.

INCREASED EXCRETION OF VITAMIN C (CEVITAMIC ACID) IN THE URINE DURING INDUCED MALARIA INFECTION. F. PLAUT, M. BÜLOW and K. F. SCHEID, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:473 (Jan.) 1936.

Six cases of dementia paralytica were studied to determine the amount of excretion of vitamin C in the urine before and during induced malaria therapy. During malarial fever the output of cevitamic acid in the urine was from three to four times the normal. As soon as the fever was checked by quinine, the amount of vitamin C in the urine was decreased. The loss of vitamin C in the urine conforms with the fact previously established that the vitamin C content of the spinal fluid becomes diminished during malarial infection. The loss of vitamin C during the acute infection may be significant, in view of the recognized anti-infection potency of vitamin C. This loss may predispose to secondary infection, and even lower resistance to the malaria. The authors recommend, therefore, that before inoculation and during the fever ample vitamin C be given the patients in the form of orange and lemon juice and fresh vegetables, and even pure cevitamic acid.

SAVITSKY, New York.

A PARTIAL ABDOMINAL REFLEX OF PATHOLOGIC TYPE. G. H. MONRAD-KROHN, Acta psychiat. et neurol. **12**:97, 1937.

Monrad-Krohn describes a pathologic abdominal reflex confined to the lower abdominal muscles, consisting of downward displacement of the umbilicus without lateral deviation. This was observed in a case of syringomyelia associated with paraplegia and total sensory loss below the third thoracic segment. This pathologic abdominal reflex could be elicited from a wide area, beginning at the level of the umbilicus and extending downward to the distal portions of the lower extremities. The optimal reflexogenic zone corresponded to the upper third of the anterolateral aspect of both thighs. From this area practically any stimulus (light touch, gentle rubbing, pinching or cold) easily elicited a reflex response consisting of downward displacement of the umbilicus. Instead of a uniform retraction reflex, a limited infra-umbilical response was elicited. When evoked from the distal parts of the lower extremities, this infra-umbilical response was accompanied by a slight shortening reflex of the stimulated leg. Monrad-Krohn explains the abnormal abdominal response by the fact that the peripheral neurons concerned in the supra-umbilical component of the total retraction reflex are destroyed by the lesion involving the corresponding thoracic segments of the cord, whereas the anterior horn cells and ventral roots in the segments corresponding to the infra-umbilical myotomes are intact or partially preserved.

YAKOVLEV, Waltham, Mass.

Cerebellum and Brain Stem

TOPOGRAPHIC SYNDROMES OF THE CENTRAL VESTIBULAR PATHWAYS IN MAN. J. A. BARRÉ, Rev. d'oto-neuro-opht. **15**:353 (May) 1937.

Barré accepts the otologists' definition of the vestibular system, using the term "peripheral" for the end-organs and the part of the nerve lying within the temporal bone and the term "central" for the rest.

I. Syndromes of the vestibular nerve are classified as: (*a*) syndrome of pressure due to tumor of the acoustic nerve, (*b*) irritative syndrome of the vestibular nerve and (*c*) syndrome of complete deficiency of the vestibular nerve. The syndrome of compression is characterized by a sensation of pulsion, sometimes inclination, of the head toward the affected side, vertigo at times, spontaneous nystagmus to the sound side, deviation of one or both arms and slight deviation of the body toward the diseased side. Labyrinthine reactions of the affected side are absent with the caloric test, normal or reduced with rotation and normal with galvanism. The reaction of the sound side to the cold caloric test is horizontal nystagmus, which may or may not be convertible into rotatory nystagmus; with the warm caloric test there is horizontal nystagmus, transformable into rotatory nystagmus by inclination of the head, and with rotation and galvanism the reactions are normal.

A pure irritative vestibular syndrome has not yet been demonstrated. In cases of serous arachnoiditis of the internal auditory meatus, for example, signs of irritation (tinnitus, rapid diminution of hearing, violent vertigo and marked caloric hypereflexia) are associated with signs of deficiency. In the syndrome of complete deficiency there is total areflexia with all tests. Areflexia with the galvanic test indicates profound degeneration of the vestibular nerve.

II. As syndromes of the bullae segments of the vestibular pathways, Barré discusses tumor of the cerebellopontile angle, syringobulbia, the unilateral bulbar syndrome and multiple sclerosis.

A. In cases of tumor of the angle, with compression of the bulb, lateropulsion is marked and is often supplanted by titubation and, finally, by falling. Later vertigo is less frequent than in the initial stages. Nystagmus is toward the sound side, but sooner or later it changes in direction toward the diseased side, while the arms and the body continue to deviate in the original direction. Signs of nystagmus often vary according to the direction of gaze. The caloric test causes no reaction on the diseased side, except deviation at times of the trunk and arms. The cold caloric test on the sound side often results in horizontal nystagmus, with or without rotatory transformation. With the warm caloric test on the sound ear, horizontal or horizontal-rotatory nystagmus to the sound side may be produced. The results of the rotation test are variable. The sense of rotation during turning is often preserved. With the galvanic test reactions may sometimes be obtained from both sides.

B. In the irritative type of the vestibular syndrome resulting from syringobulbia, the nystagmus is rotatory, but may be horizontal or mixed. The intensity is often marked and varies with change in gaze. It increases when the patient looks downward and in the direction of the quick component. Vertigo is not frequent. Lateropulsion is often observed, but is soon compensated; sometimes a staggering gait persists. There is deviation of the arms to the same side as that of the trunk. Reactions to the vestibular tests are usually normal; the threshold of stimulation is often low, and spontaneous nystagmus is easily reversible. The lesions of syringobulbia produce, as it were, experimental section of the acriform fibers, which plays a dominant part in the genesis of rotatory nystagmus.

C. Vestibular disturbances in the unilateral bulbar syndrome of Wallenberg are of two types. In the first the nystagmus is rotatory, and in the second, horizontal. In the first type the nystagmus is usually toward the side opposite the lesion; it appears suddenly and becomes less intense as time progresses. It may change in form when the patient looks to the opposite side. In the second type, when the lesion is low, at the inferior part of the descending root of the eighth nerve, the nystagmus is rotatory and is produced by alterations in the domain of the posterior inferior cerebellar artery. When the lesion is higher, in the region of the lateral fossette of the bulb (Foix and Hillemand), the nystagmus is horizontal and behaves as does that of the first type. Spontaneous, pathologic rotatory nystagmus is indicative of an irritative central lesion; it seems not to depend on special excitation of the vertical canals. The transformation of provoked horizontal into rotatory nystagmus disappears in association with numerous lesions of the cerebral trunk, especially those located in the lower portion.

D. The striking feature of the vestibular disturbances associated with multiple sclerosis is the marked predominance of subjective and irritative phenomena over those of deficiency. Vestibular disturbances are sometimes the earliest to appear; it is particularly important to recognize them when they are unilateral. In early stages there is vestibular hyperexcitability, but in more advanced disease the threshold is normal in 60 per cent of cases.

III. Three syndromes of the pontile segment of the vestibular pathways are described: vestibular disturbances in the syndromes of Foville; a pontile vestibular syndrome without disturbance of ocular motility ("pure crossed vestibular dysreflexia"), and abolition of vestibulo-ocular reactions, with conservation of vestibulospinal reactions. In the first type, represented by a case reported by Van Gehuchten, there were paralysis of lateral movements of the eyes, facial paralysis, vertigo, nystagmus and deviation of the body, caused by a tuberculoma of the left half of the pontile tegmentum. Instrumental tests revealed marked diminution of vestibular excitability on the left side. In the second type the syndrome reproduced the findings observed by Leidler and others in animals after extirpation of a cerebral hemisphere. Barré called this syndrome pure crossed vestibular dysreflexia and reported a typical case in 1935. The patient had a lesion on the right side. The various tests produced nystagmus to the right only, and the slow phase of the nystagmus was always to the same side as deviation of the arms and body. Bard's assumption that there is a chiasm of the central vestibular pathways is substantiated by this case. In the third type, abolition of vestibulo-ocular reactions with conservation of vestibulospinal reactions, is represented by a case of syphilitic arteritis, with bulbopontile complications and facial paralysis of the side opposite the lesion. There were no vestibular symptoms. With the cold and warm caloric tests no nystagmus was provoked, but reactional movements of the arms and body were correct. The lesion of the bulbopontile tegmentum had sectioned the vestibulo-ocular fibers and spared the deiterospinal fibers, thus conserving all the reflexes below it. No vertigo was produced by the tests. Except for the absence of vertigo, the findings corresponded exactly to the schematic syndrome which Jones stated to be characteristic for a lesion of this region.

IV. Syndromes of the annexed bulbar and pontile regions are described.

A. Barré classifies the vestibular disturbances associated with tumors of the fourth ventricle as the global syndrome and sydromes of the central region of the ventricle, the lateral recess and the inferior and superior angles. The central and global syndromes of the floor of the fourth ventricle are characterized by hypersensitive vestibular reactions to all tests. In the later stages there are diminution and eventual abolition of provoked vertigo and nystagmus, while provoked deviations are conserved and correct. Spontaneous vertigo and staggering are marked.

The syndrome of tumor of the lateral recess resembles that of tumor of the cerebellopontile angle, with the following differences: In cases of tumor of the lateral recess there are usually precocious vomiting and unilateral tinnitus with normal hearing and pain in the region of the fifth nerve on the same side. Vertigo may be absent, but there is lateropulsion to the diseased side, followed by staggering and falling. The results of instrumental tests are not known.

The vestibular syndrome of the bulbar triangle of the floor of the fourth ventricle is illustrated by a case in which there was complaint of hiccup, difficulty in swallowing, insomnia and complex nervous crises of the bulbocervical type. There were bilateral tinnitus with hypacusis, vertigo, lateropulsion, deviation of the body to one side and vertical nystagmus on looking downward. Reactions to vestibular tests were normal. There were no signs of hypertension. The vestibular syndrome of tumor of the superior angle of the floor of the fourth ventricle resembles that of tumors of the aqueduct and of the valve of Vieussens. There is no spontaneous nystagmus or lateropulsion, and objective reactions to instrumental tests are normal, with a low threshold. Early spontaneous vertigo of short duration, with absence of provoked vertigo to normal instrumental tests, is particularly associated with compression of the upper part of the fourth ventricle.

B. Vestibular disturbances in tumors of the cerebellum are absence of vertigo and exaggeration of nystagmic reactions, characteristic of tumors of the posterior fossa. In cases of tumor of the vermis marked disturbance of equilibrium, with correct past pointing, is often observed. Vestibular disharmony is contemporaneous with other signs of cerebellar involvement in cases of abscess of the cerebellum. With cerebellar tumors the sign of vestibular disharmony is frequently observed. While this disharmony signifies disturbance of the central vestibular pathways, Barré has always found it associated with disease of the cerebellum. He has observed it also in cases of lesion of the peduncular tegmen.

V. Syndromes of the peduncular portion of the vestibular pathways are modified by the various locations of the lesion in the mesencephalon. Typical observations are spontaneous vertical nystagmus, long duration of the provoked nystagmus, difference in the threshold for the slow and that for the rapid phase of nystagmus; nystagmus of different types and amplitudes in the two eyes, and nystagmus retractorious (rare). Vestibular disturbances are often coincident with disturbance in ocular motility of nuclear, supranuclear or peripheral origin. Optokinetic nystagmus is frequently absent entirely or in one direction. Provoked rotatory nystagmus is often absent, sometimes in one eye only, as is inversion of nystagmus when the head is inclined anteriorly. In a large number of cases the vestibulospinal reactions are normal while the vestibulo-ocular reactions are disturbed, but sometimes the former participate on deviation upward of one or both arms or the knee. Perhaps such instances represent a vestibulo-equilibratory complex. The diverse phenomena observed in the syndrome of the peduncular region become clear when it is realized that they are manifestations of lesions involving the posterior longitudinal bundle or its fibers of distribution and the oculomotor pathways in their supranuclear, nuclear or peripheral segments.

In cases of tumor of the third ventricle vestibular disturbances consist of vertical and horizontal nystagmus.

VI. Vestibular disturbances in disease of the pallidum have been discussed in connection with epidemic encephalitis lethargica. Muskens has assigned to the pallidum the role of a superior vestibular center.

VII. Vestibular disturbances associated with lesions of the frontal pole were described by Delmas-Marsalet. Barré suggests that phenomena belonging to the equilibratory apparatus should be differentiated from those belonging to the vestibular apparatus. He doubts whether the frontal pole exerts direct influence on the vestibular apparatus. The frontal type of past pointing arises from the pyramidal system.

VIII. Vestibular disturbances have been described in cases of tumor of the temporal lobe, but none in other diseases of the temporal lobe. An important characteristic is the great variability of the vestibular phenomena, such as spontaneous past pointing in patients with perfect equilibrium as well as in those with marked disequilibrium. Spontaneous past pointing of the type characteristic of lesion of the frontal or the temporal lobe does not exist. The thresholds for nystagmus are equal on the two sides and are usually normal. In almost all cases in which there is hyperexcitability the onset is recent. Provoked vertigo is feeble or absent.

IX. Vestibular and equilibratory disturbances associated with tumor of the parietal lobe are characterized by absence of spontaneous nystagmus, frequent and, at times, violent disequilibrium consisting of retropulsion and lateropulsion, similar to that observed in the tumors of the frontal and temporal regions. The provoked nystagmus has a low threshold, large amplitude, high rapidity and long duration and is, in some cases, interrupted by a slow tonic movement that brings the eyes into a lateral position. Sometimes conjugate deviation of the head and eyes is observed. Provoked vertigo is relatively slight. Optokinetic nystagmus may be irregular or may be absent in some direction.

DENNIS, San Diego, Calif.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

MEYER SOLOMON, M.D., *President, in the Chair*

Regular Meeting, Nov. 18, 1937

A CASE OF CHRONIC SUBDURAL HEMATOMA WITH ACUTE MANIFESTATIONS. DR. D. M. OLKON.

The interest in this case of proved chronic subdural hematoma lies in the acute manifestations of psychotic behavior associated with only minimal neurologic signs.

A white man aged 37, married, of good health and exemplary habits, alert and actively engaged in business, was on his vacation, when suddenly acute symptoms developed. He became confused and completely disoriented as to time, place and person, failed to recognize his wife and immediate family and became violent. He refused food and water for fear that they were poisoned and expressed many hallucinations and delusions; e. g., he thought that persons were standing over him with guns to kill him. He was fearful of every one near him and became negativistic, anxious, apprehensive and resistive.

When taken to a hospital, he walked out in his pajamas and had to be brought back with the aid of the police. On his return to the hospital he became greatly disturbed, screaming that he wanted to die. He still refused food and, as a result, became very weak. The physician in attendance believed his condition to be an acute psychosis and advised his return to Chicago for institutional care.

I saw the patient on July 31, 1937, four days after the acute onset. The history given by relatives included the observation that during the past year there had been a marked change in personality. Formerly he had been a person of exemplary habits and good disposition. Now he became quarrelsome without particular provocation, avoided his former friends and companions, became secretive and faultfinding and had the idea that his superiors in business "were not giving him a square deal." After work he refused to go out of the house and never seemed to have enough sleep. He complained of frequent headaches and a feeling of tightness in the head. Appetite became poor; he became capricious about his food and lost considerable weight. He did not vomit. In June 1936, while driving a car in the daytime he had suddenly felt a sensation in the head, as if he had been struck with a hammer. He became confused, dizzy, tired and weak, and felt great pain in the head. He stopped the car, rested for a time and then drove home. He complained of a "pounding headache" and weakness. A physician thought that the patient had suffered from sunstroke and prescribed a tonic for weakness and bromoseltzer for headache. The patient's general condition improved, but the headaches continued. For these he took bromoseltzer three or four times a day, without improvement. In the winter of 1936 and 1937 the patient had had a tendency on several occasions to stumble and fall. To these occurrences he had paid no particular attention.

When seen on July 31 he was confused, apprehensive and irrational. He did not know his age or where he was and did not recognize his family. He refused examination and did not talk spontaneously. He started to undress in the presence of women and seemed unconcerned about it. His face was pale and masklike. His lips were covered with sores, and the breath had a fetid odor. In walking he staggered to the right. Because of resistiveness, it took three men to get him into a car.

Examination in the hospital revealed: cold, clammy, pale skin; temperature, 98.4 F.; pulse rate, 80, and respiratory rate, 24. The heart and lungs were normal. The blood pressure was 110 systolic and 70 diastolic. The tonsils were reddened, and the tongue was dry and coated. The abdomen was soft and without palpable masses. The prostate was small, smooth and soft. The patient was now in a daze and did not respond to questions or to painful stimuli. He lay in bed completely immobile and soon passed into a semistuporous state. He repeatedly muttered: "Death—killing—no use—I am dead—take them away." During the night he became restless and wanted to get out of bed and jump out of the window.

Neurologic Examination.—The pupils were round and equal; they were about 4 mm. in size and reacted well to light and in accommodation; the eyegrounds appeared normal. There was no paresis or paralysis of the extra-ocular or facial muscles or rigidity of the neck. The deep reflexes of the upper and lower extremities were present (about 2 plus) and equal on the two sides. The right knee reflex at times, however, appeared a little livelier. There was no Babinski, Oppenheim, Chaddock or Rossolimo sign, no foot clonus and no paralysis in any muscle group. The grasp reflex was absent. Sensation could not be determined; there was no reaction to tactile, thermal or painful stimulation. The abdominal and cremasteric reflexes were not obtained on repeated examinations.

Laboratory Findings.—Examination of the urine and feces on many occasions revealed nothing abnormal. The blood contained 5,400,000 erythrocytes, 8,700 leukocytes and 85 per cent hemoglobin (Dare). A differential count revealed 51 per cent polymorphonuclears, 46 per cent lymphocytes and 3 per cent monocytes. Five other examinations gave similar results, except that the number of erythrocytes fell to 4,500,000. The Widal test gave negative results. There were 109 mg. of sugar and 23.43 mg. of urea nitrogen per hundred cubic centimeters of fasting blood. The Wassermann and Kahn tests were negative. The spinal fluid on puncture came in drops and was clear, without apparent increase in pressure. Examination revealed: 5 cells per cubic millimeter; Pandy reaction, negative; Ross-Jones reaction, negative; sugar, 85.42 mg.; total protein, 0.48 Gm. per hundred cubic centimeters; Kahn and Wassermann reactions, negative, and colloidal gold curve, 1111000000.

In roentgenograms the tables of the skull showed no evidence of increased pressure or erosion, or of fracture. All the sinuses were clear; the sella turcica was normal.

The patient's condition did not improve with conservative methods of treatment. While there were no definite organic changes, the antecedent history, acute onset, former constant headaches and present stuporous condition led me to think that there was organic involvement of the brain, and I advised ventriculography.

Dr. Eric Oldberg performed ventriculography on the seventh day after admission. On trephining he reported: "There is no pressure." However, as he nicked the dura for insertion of a cannula, several ounces of dark blood gushed out. The patient passed into shock, but when the head was lowered the condition improved. The cannula was inserted for about 3 cm. before brain tissue was encountered, an index of the degree of compression of the brain. When the patient was returned to bed, he complained of headache, but soon relapsed into a stuporous condition, in which he remained for three days. From then, improvement was steady. The sensorium cleared; he had no delusions or hallucinations and became affable. On the twenty-first day after admission he was discharged. After a month's rest, he returned to work on October 1, entirely well. There were no sequelae except the continued absence of the cremasteric reflex. The patient does not remember anything of the entire episode.

A few outstanding points may be restated: 1. The main symptom was acute psychosis without dominant neurologic findings. 2. The change in personality antedated the acute onset by about a year. 3. The subdural hematoma was not due to alcoholism, syphilis, cardiovascular-renal disease, diabetes, trauma or any

known etiologic factor, and was chronic in character. 4. Proper drainage of the hematoma produced complete recovery. 5. Careful search of the literature did not reveal cases of chronic subdural hematoma in which the mental symptoms predominated and organic neurologic signs were mainly absent.

DISCUSSION

DR. PAUL C. BUCY: I am convinced that in a high percentage of cases of subdural hematoma there are present, as a prominent symptom, certain psychotic manifestations or mental aberrations. I think that this should be stressed. I am also convinced that many such hematomas are spontaneous. Trauma does not play a role in all cases of this kind. It should also be borne in mind that subdural hematoma is a not uncommon observation at necropsy in hospitals for mental disease. Patients with this condition rarely present evidence of organic neurologic disease.

DR. D. M. OLKON: I am aware that subdural hematoma is not a rare observation at necropsy. In this instance, however, the almost complete absence of neurologic signs, the acute psychotic manifestations and the presence of a chronic subdural hematoma, which was least suspected, make the case outstanding.

ANATOMIC BASIS OF THE THALAMIC SYNDROME. DR. A. E. WALKER (by invitation).

The spinothalamic tract and its trigeminal equivalent, the dorsal secondary trigeminal tract, terminate in the basal posterior portion of the lateral nuclear mass of the thalamus with a specific arrangement. The fibers from the spinal root of the trigeminal nerve terminate medially; those from the sacral portions of the spinal cord, laterally, and those from the cervical regions, in the intermediate portion. The medial lemniscus and the ventral secondary trigeminal tract end in the ventral portion of the posterior moiety of the lateral nuclear mass, which receives the terminations of the spinothalamic and lemniscal tracts and projects exclusively to the postcentral convolution. Both projections have a similar topical organization. The fibers which arise in the medial portion of the lateral nuclear mass terminate in the inferior parts of the precentral and postcentral gyri; those from the lateral part, in the superior portions, and those from the intermediate part, in the middle of these convolutions. Thus, there is maintained throughout the entire sensory system a precise organization of the body segments.

This insight into the thalamic organization allows an appreciation of the anatomic basis of some thalamic syndromes. The classic syndrome is the result of a lesion of the posterior portion of the lateral nuclear mass, which causes severe sensory disturbances by involvement of the part of the thalamus in which the spinothalamic and lemniscal tracts terminate. The dissociation of sensibilities is probably dependent on the numerous other connections (with the pons, mesencephalon and midbrain) made by the spinothalamic system. Lesions of the anterior portion of the thalamus, usually due to thrombosis of the perforating thalamic artery, produce little sensory disturbance, but tremor, ataxia and choreoathetoid movements of the contralateral extremities, especially the upper, are prominent. These insults involve the part of the thalamus in which the fibers of the brachium conjunctivum find termination. Hence, it is not surprising that a lesion in this region produces signs and symptoms which are usually associated with cerebellar disease. Occasionally, small lesions of the thalamus are present, displaying only a fragment of the aforementioned syndromes, depending on the portion of the thalamus involved.

DISCUSSION

DR. ROY GRINKER: I compliment Dr. Walker on the result of his research and have only one question to ask. He stated that he believes that thalamic hyperpathia is due not to a release phenomenon but to an irritative process. It

is difficult for me to understand the process of continuous irritation over many years. If the lesion is intrathalamic and no lesions are seen in the cortex, why is not the release phenomenon intrathalamic, and why must one not postulate an inhibitory function for certain thalamic structures, especially since the hyperpathia is not spontaneous but is brought out by slight external stimuli?

DR. A. E. WALKER: There may be many explanations for hyperpathia. Certainly, the question is not solved. However, there are several reasons for thinking that cortical, or even intrathalamic, inhibition is not responsible. I mentioned that patients whose entire cortex has been removed do not have these pains; yet if the thalamus of such patients behaves as does that of the macaque monkey and the chimpanzee, practically all the cells of the lateral nuclear mass are degenerated. It seems that if these cells exert an inhibitory influence on other parts of the thalamus such degeneration would release it, and give rise to hyperpathia. This, however, does not occur. If one can argue from other types of spontaneous discharge within the central nervous system, such as the traumatic epilepsy which one considers to be due to the influence of a scar, I see no reason that a similar lesion of the thalamus might not discharge and give rise to pain.

RABIES VACCINE IN TREATMENT OF EPILEPSY. DR. ISIDORE FINKELMAN, DR. A. J. ARIEFF and DR. M. A. SCHILLER (by invitation).

Antirabies vaccine was administered to 13 patients suffering from epilepsy. Each received twenty-one doses, administered daily, and some were given a second course of treatment. There was no change in the frequency or severity of the seizures, except that in one case attacks ceased for two months and then recurred. All patients have been observed for at least six months subsequent to the treatment.

THE PROBLEM OF OUTPATIENT PSYCHIATRIC SERVICES IN COOK COUNTY, ILL. DR. CONRAD S. SOMMER.

The efficient organization of medical and welfare services in large urban communities is especially difficult because of the complexity of serving a very large population, with many and complex needs. In such situations there is an urgent need for the interested agencies to view the community and its problems as a whole if comprehensive solutions are to be obtained. This paper attempts to contribute to the integration of the psychiatric outpatient services of Cook County by surveying the need for such facilities and the facilities actually available.

The standard of the services for all classes of psychiatric outpatients of 1 psychiatrist, 1 psychologist and 2 or 3 psychiatric social workers for each 100,000 of the population is discussed as meeting the indispensable needs of American communities. Cities can pay for this amount of psychiatric service without neglecting other needed medical and welfare services. According to this standard, Cook County should provide its psychiatric outpatients with the full time of at least 40 psychiatrists, 40 psychologists and 100 psychiatric social workers. The equivalent of the full time of only 24 psychiatrists, 21 psychologists and 39 psychiatric social workers is available. This is about one half of the standard discussed.

A survey of several social agencies indicates that the community yearly discovers thousands of adults needing and capable of benefiting from psychiatric treatment for whom no facilities for such treatment are available. A study of the psychiatric clinics indicates that these clinics alone discover yearly hundreds of persons who need and are capable of benefiting from psychiatric treatment for whom therapeutic facilities are not available.

There is a geographic maldistribution of clinics in the county. Large industrial areas are located at prohibitive distances from the present clinics. This situation could be remedied by the establishment of additional branch clinics of the Institute

for Juvenile Research, of dispensaries in peripherally located general hospitals, of additional psychiatric services in local school systems or of psychiatric dispensaries in district health centers.

An insufficiency in certain types of personnel exists in some clinics. A common finding is insufficient psychiatric social service. The Chicago school system has made commendable and rapid expansion in the employment of many psychologists, without, however, providing for an accompanying increase in psychiatric or psychiatric social services.

The practices of the clinics in regard to admissions too often fail to provide a liberal policy for the admission of psychiatric patients.

Procedures of treatment are often influenced by such considerations as teaching, research and the pressure of a heavy case load. Efficient care is given to patients who can be handled by the judicious administration of sedatives, advice and encouragement. Adults whose neuroses could yield to more intensive therapy too often do not receive it.

There is need for the further expansion of the present facilities for the careful supervision and orderly training of young psychiatrists entering dispensary practice. Such an expansion would lead to elevation of the standards of training and experience of personnel in the clinics. There is need for more facilities to pay psychiatrists for their services in clinics if the service needs of dispensary patients are to be met.

The closer collaboration of psychiatrists and physicians in other medical specialties is leading to more effective handling of the problems of the psychoneuroses.

The establishment of a new psychotherapeutic clinic for adults to serve as a community experiment and demonstration in effective, economical, short time psychotherapy is proposed.

In conclusion, it is pointed out that the community has made some progress in attempting to view its psychiatric problem comprehensively. It has organized itself fairly well for the hospital and custodial care of the mentally ill. It is in the process of organizing itself more comprehensively in regard to research and undergraduate and graduate education of physicians in psychiatry, through the endeavors of the Council for Psychiatric Research. There are needed a comparable organization and integration of community planning to attack the problem of securing mental health by provision for effective psychiatric outpatient services commensurate with the needs of the community.

DISCUSSION

DR. RALPH HAMILL: I should like to speak in favor of this report and to ask for its consideration by members of this society. It is, of course, a demand on the medical profession toward which leaders of the profession, one may say, are not sympathetic. It strikes me as important. The problem of psychotherapy or of an outpatient department of psychotherapy demands a degree of patience and sacrifice for which it is impossible to ask without remuneration. The plan outlined by Dr. Sommer has been arrived at after serious consideration of the need for psychiatric treatment rather than that for mere psychiatric diagnosis, and I again plead for some recognition of it.

DR. ROY GRINKER: I think no one has really been cognizant of the actual situation in the city, as portrayed by Dr. Sommer. All have felt that psychiatric work is quantitatively, and often qualitatively, very poor, but the actual situation he has demonstrated, after thorough investigation, is appalling. We as physicians have adopted an attitude of *laissez faire* toward the whole matter and have had the impression that the agencies now established are doing the best they can and that one may hope for gradual improvement as a result of education. It seems to me that things are progressing too fast elsewhere for us to stand by and allow the situation in Chicago to continue. One particular point may drive this home. A large number of persons who need psychiatric care can pay only minimum fees

—a very few dollars. They are not accepted by the clinics or by the private physician, and any effort to organize a clinic to take these patients is met with resistance by organized medicine; every effort to get them into the hands of private psychiatrists is met with approval. These patients have not sufficient funds for adequate private care, and hence are poorly treated or not at all. For these persons a great deal can be done by the establishment of paid psychiatrists in new or existing clinics. It seems that we can take a step forward in a constructive way by working with the Society for Mental Hygiene and by giving the organized auxiliary agencies as practicing psychiatrists our impression and point of view on this problem.

DR. PAUL C. BUCY: I approach this problem not as a psychiatrist but as a layman. I wish to ask these questions not in a sense of criticism but in the hope of clarifying the situation for myself. I realize that in raising these questions some will assume that I have adopted an attitude typical of a surgeon. I wish to ask Dr. Sommer to what extent in making this survey he has considered the facilities which are made available by practitioners in private practice. What evidence is there that these supposedly untreated patients would be benefited or that the community would be benefited by their treatment? One cannot take the word of a social worker or of a social agency that treatment would be beneficial to the patients who are now cited as untreated. Why should the community express unusual concern for them, out of proportion to that it expresses for the ordinary medical patient? What evidence is there that the community will achieve a return commensurate with the required financial outlay? Dr. Sommer mentioned the inadequate treatment now commonly carried out—conversation with the patient, a certain amount of advice and the prescribing of sedatives. What would he consider advisable and adequate treatment, and what would be the benefit of the additional therapy which he proposes?

I think Dr. Sommer made an erroneous assumption, one which will prove disastrous to any plan providing for care of the psychoneuroses, that is, that the problem is largely one for the psychiatrist and that the psychiatrist does now and should care for all or most of the psychoneuroses. That is not true; it never has been true and never will be. The great mass of patients with these disorders are cared for by the general practitioner and by specialists in such fields as internal medicine or surgery. That always will be true. There are surgeons, there are internists and there are psychiatrists who are not sympathetic toward the problems, emotional and otherwise, of the psychoneurotic person. There is, however, a larger proportion of the medical profession which is sympathetic and is aware of the necessity for considering, and does consider, the emotional state of the patient, whether he has an organic disease or not. Any plan which proposes to have all psychoneuroses cared for by psychiatrists or psychiatric clinics will fall of its own weight. The problem is too big. It must be the concern of the entire medical profession. It seems that, like the problem presented in improvement of obstetric care, it is largely one of educating the entire profession rather than one of establishing a few clinics to care for a handful of patients.

DR. J. KASANIN: I think Dr. Bucy is right in saying that most patients who are psychoneurotic are treated by general practitioners. The point is this: The practitioner has a certain amount of time and a certain amount of patience. When the patient becomes too difficult he is referred to the psychiatrist. Patients with psychoneuroses take a good deal of time. The psychiatrist may use suggestion, psychotherapy or psychoanalysis—he may use anything. In outpatient work one tries to see the patients frequently; yet there are so many that one cannot accomplish this purpose. I believe that in order to get results one must give a good deal of time to these patients.

Perhaps in some cases this is an illusion; in others it is true. For this reason I believe that Dr. Sommer's proposal merits consideration. If one can establish a modern clinic, I think that that would be of great benefit to the community and of great value to research in studying methods of psychotherapy, of which there are only vague notions at present.

DR. CONRAD S. SOMMER: I appreciate the several discussions and believe they have been helpful. The question arises how much time can be given from private practice for the care of patients who require many fairly lengthy interviews. I have sent out a questionnaire to neuropsychiatrists of this community asking how much time they could devote to a patient paying $3 an hour. Some said one hour; some, thirty minutes, and others, as much time as is needed. However, the practice has actually been that a patient of this kind, unless he is unusually interestnig from a clinical point of view, is too often dropped. One cannot be sure of continued treatment when a patient can pay only $3 or less per hour, and the practitioner can hardly afford to keep office hours if he is paid such low fees. The Society for Mental Hygiene has for a long time attempted to induce psychiatrists to take patients who can pay very little and the psychiatrists have cooperated, but they do not seem to be able to see many of these patients for long at $1 or $2 an hour. Dr. Bucy raised the question of social workers determining the need for psychiatric treatment. In almost all instances the need is determined by psychiatric examination. He also raised the question: Why should psychiatric cases be stressed more than those of other medical specialties? They should not, but it was pointed out that a community can pay for the services of 1 psychiatrist, 1 psychologist and 2 or 3 psychiatric social workers per hundred thousand of population without neglecting its other medical and welfare services. If a community is neglecting its medical services, it is up to the psychiatrist to see that this specialty is taken care of, without, however, doing so at the expense of other needed services. I hope that I have not given the impression that treatment by sedatives and advice is inadequate—by no means—but there is a type of patient in the dispensaries who often does not get the more intensive therapy that can help him to adjust. I do not think that psychiatrists see the majority of the patients with psychoneurosis. However, through the psychiatric consultation services in the hospitals, surgeons and other specialists are now taking a more effective interest in psychoneurotic patients.

There are some such clinics—not quite like the one proposed, but similar. The Tavistock Clinic, in London, cares for inpatients also and has had satisfactory results. The Cornell University Medical College has done good work of this kind, not only in psychiatry but in the other specialties. The physicians are paid in that clinic. The department for ear, nose and throat diseases can make money and help defray the expenses of the psychiatric department. Because psychiatric interviews and treatment take so much longer, their cost is enough greater to make it incumbent on dispensaries to establish admission practices for psychiatric patients that are more liberal with regard to the patient's economic status than are the standards set up for the ordinary medical patient.

MEYER SOLOMON, M.D., *President, in the Chair*

Regular Meeting, Dec. 16, 1937

HISTOPATHOLOGIC CHANGES IN THE BRAIN IN CONVULSIONS EXPERIMENTALLY INDUCED WITH METRAZOL. DR. ARTHUR WEIL and DR. ERICH LIEBERT (by invitation).

The effect of metrazol on the central nervous system was studied in a series of 18 rabbits. In order to imitate its therapeutic application in dementia praecox, the dose was established which would produce a convulsive seizure, and this dose was injected twice a week. The mean convulsive dose was from about 12 to 18 mg. per kilogram of weight. The rabbits were either killed at the end of each experiment or were allowed to live for various periods. Histopathologic changes in the central nervous system were noticed only in the rabbits which had received a total of 700 mg. of metrazol or more. These pathologic changes were

mostly mild, consisting of shrinkage of the nuclei and cytoplasm of ganglion cells in various regions. Here, too, as in rabbits in which insulin shock was produced, the changes in the peripheral part of the cornu ammonis were more pronounced than those in the central part.

If the values found for the rabbit are calculated for a man with the average weight of 60 Kg., one may conclude that a total of 13.5 Gm. of metrazol injected twice a week for five weeks is the maximal cumulative dose which may be given to a patient without producing histologically demonstrable pathologic changes in the central nervous system.

DISCUSSION

DR. A. A. LOW: If Dr. Weil's charts refer to human beings as well as to the experimental rabbit, I must have crippled or killed a number of patients. Of course, Dr. Weil did not present his observations as strictly comparable with clinical conditions. His work, however, if substantiated by further research, implies criticism, and perhaps indictment, of the insulin shock treatment.

As was pointed out, one does not see as many convulsions in patients treated with insulin shock as in rabbits in which shock is induced experimentally. The pathologic changes in rabbits may, then, be due to the convulsions rather than to the insulin medication. This may give some comfort to the clinician. However, Dr. Weil's charts show that some of his rabbits presented severe damage even when the convulsions were few. Moreover, his results with metrazol shock demonstrate that the convulsions alone are not responsible for the pathologic changes. The rabbits treated with metrazol, with numerous convulsions, presented hardly any pathologic changes. I admit that I am perplexed. If comparable damage was done to our patients, why were my colleagues and I unable to detect evidence of it in examinations made between the treatments and afterward? Yet we were unable to discover any symptoms referable to the central nervous system. Other observers have had the same experience.

Are the changes demonstrated by Dr. Weil really irreversible? Similar changes in the ganglion cells were obtained by Schmidt, but he considered them reversible.

DR. PETER BASSOE: Some time ago, some one said that there is reason to believe that the insulin treatment may cause parkinsonism. I wish to ask Dr. Weil if he has seen changes in the basal ganglia that indicate such a possibility.

DR. ROY GRINKER: Dr. Low has brought up a question of great importance. Many hundreds of patients have and will be given some form of shock therapy. Up to the present, sufficiently accurate and detailed physiologic and psychologic studies have not been made before and after therapy. It is not necessary to have a gross neurologic defect as the result of histologic changes which might occur in the human patient comparable with what Dr. Weil has demonstrated in the rabbit. However, such damage should be demonstrable by means of careful psychologic testing. The possibility that structural defects are created by shock therapy raises the question whether the beneficial results are similar to those reported by Moniz and Freeman after the horrible leukotomies that they performed on the frontal lobe. Their patients were said to have improved. Does shock therapy improve schizophrenic patients by structural damage of a less intense, but more diffuse, type? This question can be answered by careful studies on patients subjected to experimentation—studies which are not yet available.

DR. ARTHUR WEIL: Dr. Low said that, in his opinion, the severity of the pathologic changes was not proportionate to the number of seizures. That is exactly what I intended to demonstrate; one is dealing with a cumulative effect of large, toxic doses of insulin. A rabbit which had forty-five seizures and which had been hypersensitive to insulin received a total of 59 units (equivalent to 1,690 units for a man weighing 60 Kg.). No histopathologic changes were observed in this case. On the other hand, a rabbit which had only nineteen seizures and had received 207 units (equivalent to 4,800 units for a man) had severe pathologic changes in the brain.

The second question was whether the severe changes in the ganglion cells were reversible. The answer is obtained by study of the brains of rabbits which were

allowed to survive as long as eighty days. If one sees in the brains of persons with long-standing epilepsy or hyperinsulinism large areas of the cortex devoid of neurons and severe disease of the remaining neurons, or if one observes similar changes in the brains of rabbits subjected to experimental hyperinsulinism, one must conclude that the severe disease of the ganglion cells which had been demonstrated in more acute experiments was not reversible. Of course, such pathologic changes were not produced post mortem. Furthermore, the disease of the nuclei and the glial proliferation in the chronic experiments speak against the possibility that the changes were transitory; no restoration was possible.

In reply to Dr. Bassoe, I wish to mention that at the meeting of the American Neurological Association in June 1937 a paper was read by title (Keyes, Baldwin L; Freed, Herbert, and Riggs, Helena: Hypoglycemic Encephalopathy from Insulin Therapy) in which the possibility was discussed that insulin shock therapy leads to late sequelae, such as postencephalitic Parkinson's disease. It is impossible, of course, to say that insulin alone is responsible for such disease. On the other hand, Tani reported that in rabbits treated with insulin softening of the substantia nigra with generalized severe disease of the ganglion cells was observed. In our cases, too, nuclei of the striatum and midbrain were not spared from the generalized pathologic changes of the brain.

PATHOGENESIS OF THE HORNER SYNDROME ASSOCIATED WITH LESIONS OF THE BRAIN STEM. DR. BEN W. LICHTENSTEIN.

It is well known that the Horner syndrome is frequently part of the symptom complex commonly designated as the syndrome of occlusion of the posterior inferior cerebellar artery. Some authors have explained the Horner syndrome as the result of involvement of an oculopupillary center located in the lateral reticular substance of the medulla, and others, as the interruption of an oculopapillary tract which traverses the pons and the medulla. Budge observed that pupillodilator fibers emerge from the upper thoracic segments of the spinal cord and concluded that this portion of the spinal cord contains a center for pupillary reactions, which he designated the ciliospinal center.

That the ganglion cells of the thoracolumbar outflow of the autonomic nervous system are normally regulated by cortical and diencephalic impulses is known, but there is evidence that this cerebral control is primarily inhibitory. The absence of the Horner syndrome in cases of abscess or tumor of the medulla, in contrast to its frequent occurrence with vascular lesions of the medulla, is of great significance.

For convenience, the cervical portion of the sympathetic pathway may be considered as a three link chain. The central fiber, which arises in the brain and establishes synaptic relationship with the cells in the ciliospinal center, may be designated as the first link. The so-called preganglionic nerve fiber, which arises from the ganglion cells in the ciliospinal center in the lower cervical and the upper thoracic segments of the spinal cord, may be termed the second link, and the postganglionic fiber, the third link.

Determination of the reactions of the miotic pupil to cocaine and epinephrine in cases of the Horner syndrome has been especially useful in localization of the break in the sympathetic pathway. Cocaine, which produces pupillary dilatation by stimulation of the sympathetic nerve fibers, is ineffective in cases of lesion of the second or third link. Epinephrine, which normally has no, or at most a minimal, dilator effect on the pupil when instilled into the conjunctival sac, produces a marked dilatation if the postganglionic fiber or its cell is destroyed.

Many cases of the Horner syndrome were studied with the use of these drugs. In 4 cases of the Horner syndrome occurring as part of the symptom complex known as the syndrome of occlusion of the posterior inferior cerebellar artery, the miotic pupil dilated markedly in response to epinephrine and slightly to cocaine. In 1 of these cases in which the reaction to epinephrine was studied three days after onset of the syndrome, the miotic pupil dilated neither to epinephrine nor

to cocaine. Ten days afterward this miotic pupil dilated to epinephrine, which indicated that degeneration of the postganglionic fiber is necessary before the dilator pupillae muscle becomes sensitized to epinephrine.

It is my opinion that all the sympathetic fibers to the dilator pupillae muscle do not pass via the anterior cervical portion of the sympathetic chain on the carotid plexus but that some pass via the plexus on the vertebral artery. Intracranial occlusion of this vessel not only results in a focus of softening in the medulla oblongata but, by occlusion of the vasa vasorum, affects the nutrition of the nerve plexus on its adventitial sheath.

The pathogenesis of the Horner syndrome in cases of pontomedullary lesions is, I believe, the result not of interruption of a central sympathetic tract but of degeneration of the oculosympathetic postganglionic fibers in the adventitia of the vertebral artery and its branches.

DISCUSSION

DR. G. B. HASSIN: It is interesting that Wallenberg, who described his syndrome of occlusion of the posterior inferior cerebellar artery forty-two years ago, did not mention the presence of the Horner syndrome. He did mention the anesthesia on the side of the face and the ipsilateral loss of the corneal reflex but not the condition of the pupils, the pseudoptosis and the enophthalmos. The same may be said of the observations of Eisenlohr, Senator and others, who described the condition before Wallenberg. Though they did not mention the ocular manifestations, they knew that the posterior inferior cerebellar artery was affected. Such observations seem to confirm Dr. Lichtenstein's thesis that ocular manifestations may be absent in cases of softening of the retro-olivary area and that they are due to involvement of the cervical sympathetic fibers or their injury in the sheath of the cerebellar artery. On the other hand, Levinsohn, by hemisection of the medulla, produced miosis, which thus could be due only to damage to sympathetic fibers within the retro-olivary area or substantia reticularis, as mentioned by Marburg and others.

DR. ROY GRINKER: How do the fibers pass from the posterior inferior cerebellar artery to the orbit?

DR. G. B. HASSIN: That is rather a silly question. The diagrams shown by Dr. Lichtenstein are based on physiologic experiments only; no one has seen sympathetic nerve fibers in the brain or has followed their course anatomically.

DR. BEN W. LICHTENSTEIN: Miosis does occur in high cervical lesions of the spinal cord. Anterolateral cervical cordotomy, according to Foerster, results in a Horner syndrome. The miotic pupil in such cases dilates markedly to cocaine and not at all to epinephrine. The mechanism for the production of the Horner syndrome as seen in the so-called syndrome of occlusion of the posterior inferior cerebellar artery seems, however, to be different. The miotic pupil in the latter case dilates markedly to epinephrine and slightly to cocaine. This indicates involvement of postganglionic fibers.

In answer to Dr. Grinker's question as to the anatomic localization of the oculosympathetic fibers and how they reach the eye: If oculosympathetic fibers are located in the periarterial sheath of the vertebral artery, they could easily reach the pons and the gasserian ganglion and thence pass by way of the ophthalmic division of the trigeminal nerve to the eyeball.

SENILE CHANGES IN THE NERVOUS SYSTEM. KENDALL B. CORBIN, Stanford University, Calif. (by invitation).

The marked diminution in vibratory sensibility occurring after the fifth decade in man is explained by the parallel diminution in the number of nerve fibers in the spinal roots, as well as by possible cortical changes. The diminution in nerve fibers, observed in both dorsal and ventral roots, is the result of neuronal degeneration, which has been seen in many parts of the senile central nervous system. Child's suggestion that "death from old age uncomplicated by incidental, pathologic,

or other factors is essentially death or functional failure from old age of the central nervous system, or of essential parts of it" is partially, at least, substantiated by the evidence presented.

DISCUSSION

DR. RICHARD B. RICHTER: One would think a priori that the velocity of senile changes would increase with age. According to the table, there was a much greater decrease of nerve fibers from the fourth to the fifth decade than in the seventh and eighth decades. I should like to know whether Dr. Corbin has any comment on that.

DR. KENDALL B. CORBIN: I have no evidence with which to answer this question. All I can say is that the decrease seems to begin in the fourth decade and that there appears to be a definite decline in each decade thereafter. However, I do not think the number of cases is sufficient to tell whether the decline becomes more precipitous in later life. One would expect it.

NEW YORK NEUROLOGICAL SOCIETY

MOSES KESCHNER, M.D., *President, in the Chair*

Regular Meeting, Dec. 7, 1937

A SPECIFIC MOTILITY PSYCHOSIS IN NEGRO ALCOHOLIC PATIENTS. DR. SAM PARKER, Brooklyn (by invitation), DR. PAUL SCHILDER and DR. HERMAN WORTIS (by invitation).

Observation of a singular group of symptoms in Negroes led us to the conclusion that there exists in persons of this race a specific type of alcoholic encephalopathy, characterized in the psychic sphere by a clouded sensorium, hallucinations and mannerisms and in the somatic sphere by a disturbance in motility which consists primarily of retropulsions, rigidities, rhythmic iterations, turning about the longitudinal axis and playfulness imitating schizophrenic buffoonery. The clinical picture is that of an alcoholic organic psychosis, and the disease appears to lead to deterioration and death, except in mild forms, from which the patient may recover. While we have had no opportunity as yet to examine histopathologic material, the clinical picture differs considerably from that of the more common alcoholic encephalopathy, both in the mental and in the somatic sphere. This new type of encephalopathy shows a more subcortical form of motility disturbance, whereas the common type is characterized also by advanced vegetative changes. The racial factor seems to be illustrated by the observation of only 1 case of a similar psychosis in a white person.

DISCUSSION

DR. MOSES KESCHNER: Drs. Parker, Schilder and Wortis have presented an interesting report of 9 cases of alcoholic mental disease—8 in Negroes and 1 in a white patient. In 7 of the Negroes and in the white patient the clinical picture was characterized by distinctive psychologic changes and disturbances in motility. The authors apparently distinguish this group from the more common alcoholic psychoses—delirium tremens, Korsakoff's psychosis, alcoholic hallucinosis and encephalopathy—which, they say, do not differ in Negroes and in white persons. They state that the picture described is not that of the typical encephalopathy observed among Negroes but constitutes a type specific to persons of the race. It is not quite clear to me what the authors attempt to convey by this statement, especially since they state that they have no histopathologic evidence on which their thesis can be based.

According to the authors, one of the reasons that they consider the 7 cases as a specific group is a characteristic disturbance in motility which was present in

all the cases. This disturbance was in the nature of transitory rigidities, changing to cataleptic postures, retropulsion and falling backward, whirling around the longitudinal axis, rhythmic iterations in movements of the face and extremities, increase in postural reflexes, changeable pupillary reactions, paraphasias and mutism. It is also emphasized that all these disturbances in motility were changeable and often gave the impression of voluntary exaggeration and silly playfulness.

This is not surprising when it is considered that in chronic alcoholic intoxication there occur widespread structural and functional alterations throughout the cerebral cortex, cerebellum, periventricular structures, peripheral nerves and even the cord. Such changes must necessarily lead to psychosomatic disintegration with regression; this gives rise to disturbances in consciousness and awareness of muscular tension and relaxation which interfere with the normal synergic relations of the trunk, vertebral column and extremities. In the course of such disintegration, the disturbances in motility represent release phenomena, the instinctive impulses being allowed free expression as a result of the loss of normal cortical control.

It is noteworthy that in a recent paper (Bender, L. and Schilder, P.: Encephalopathia Alcoholica [Polioencephalitis Haemorrhagica Superior of Wernicke], ARCH. NEUROL. & PSYCHIAT. **29**:990 [May] 1933) there were reported 24 cases of alcoholic encephalopathy—23 in white persons and 1 in a Negro; in 20 of these cases there occurred disturbances in motility, posture and attitude similar to those seen in the group reported on tonight. Between 1906 and 1920 I had occasion to observe several thousand cases of various forms of alcoholic psychosis in white persons as well as in Negroes. Except that delirium tremens in those days was relatively rare in Negroes, there were no striking differences in the phenomenology of the alcoholic psychosis in the two races. Whatever difference was discernible occurred in the pattern of the abnormal movements in Negroes. In these patients there was observed a primitive, infantile type of motility, with a tendency to rhythmic movements and repetition. I did not regard this, however, as due to action of the alcohol directly. I was inclined to look on it as a racial factor observed regularly in Negroes suffering from chronic intoxications (from causes other than alcohol) and psychoses and neuroses, regardless of their nature and etiology.

I doubt whether it is advisable to construct a syndrome of a specific motility psychosis in Negro alcoholic patients on the basis of 7 cases in which no histopathologic studies were made but many etiologic factors and complications may have been in operation. In 3 of these cases there was evidence of syphilis; in 1, an abscess of the lung, with focal infection in the ears and gums; in 2, fracture of the skull, and in 1, extensive cardiovascular disease.

Whether or not one accepts the authors' attempt to construct such a syndrome, one must admit that their presentation is an excellent contribution to the study of racial psychopathology.

DR. H. A. RILEY: I feel much the way that Dr. Keschner does in regard to this presentation. I think it is of interest, but if the title of the paper had been: "An Interesting Kind of Motor Disorder Shown in a Group of Alcoholic Patients," it would have been closer to the facts that have been presented. I do not know what the authors mean by a "motility psychosis." Is it a psychosis of movement? If all the material is like that which was shown on the screen, I do not think they document the statements in the paper. I saw only one instance when the man was on the ground and one when he was upright in which he seemed to be revolving around the long axis. This type of movement was suggestive of the disturbances associated with disease of the semicircular canals. In all the other illustrations he was running about and turning backward somersaults around what I should call the transverse axis. I think, as Dr. Levy remarked to me, that these movements look more like those due to reversion to an infantile pattern. I know that my children, and many other children, spend hours in turning backward somersaults and rolling up and down hill about the longitudinal axis. I think it is unsafe, and not at all justified by what has been seen, to describe this move-

ment disorder as a true syndrome. I do not think it is specific enough; it does not resemble, so far as the authors have shown, any movement disorder which can be associated with a specific part of the nervous system.

I recognize in it no ordinary disturbance of motility. It appears more like a well organized pattern of motility—one to be linked with one or another of the developmental levels. It is a behavior, not a motility, disorder. I believe it would be better to call it an interesting type of movement seen in alcoholic persons rather than a specific motility psychosis.

Dr. Paul Schilder: I wish to make only a short remark about the term "motility psychosis," which has been used by the Wernicke school, especially by Kleist, to characterize movements as they are found in hyperkinetic and akinetic catatonic states, and to say that we think that this type of motility is characteristic. One must ask on what basis such a pattern may occur. Sometimes it looks as if it were merely a psychic regression, such as is seen in slightly intoxicated persons. However, in catatonic persons such a disturbance, obviously, goes much deeper, and one may see associated rigidities which I have not observed so far in normal persons when they were intoxicated. In our cases there were severe disturbances in motility. There were rigidities which corresponded absolutely to the rigidities seen in encephalopathy, but were more variable. In addition, we found disturbances in the postural reactions. Divergence of the outstretched arms, which is a normal reaction, was enormously exaggerated in these persons. At the same time, the reaction to turning the head was much increased. In addition, one finds that the patients show severe catalepsy from time to time. It is therefore correct to say that there were severe disturbances in motility. Of course, motility is not isolated; Wernicke has described psychomotor disturbances. It is important to know about this type of motility and to realize that, in spite of the fact that the picture looks like mere silliness, there is something organic behind it; it is interesting to have clinical proof at least of that. The picture has resemblances to that of excitement observed in some instances of hypoglycemic shock, in which also a severe organic disturbance is a background for what seems to be mere silliness. This point of view is important for several reasons, of which one is that it permits an organic approach to study of the disturbances which one sees in hyperkinetic catatonia. That is one of the chief reasons that we paid attention to this group of cases. In addition, we often found changing pupillary rigidities; these are also seen in catatonic persons. When one considers all these factors, one can state safely that there is here a specific type of motility with an organic background.

From the clinical point of view, in some cases a severe alcoholic psychosis of this sort has ended in a Korsakoff's psychosis, concerning the pathologic picture of which something is known. Thus, there are cortical and periventricular lesions. One is dealing with an organic syndrome, and it is interesting that the motility is a mere mannerism. I think that in cases of slight intoxication some organic disturbance is going on. The condition we have described cannot be understood from the psychologic point of view alone; there are organic factors involved. So much for the clinical and the motility picture.

The question remains to what extent this reaction is specific. After all, in the cases which Dr. Bender and I described the condition was different. The air of playfulness in the encephalopathy under discussion is not as outstanding in other forms. We believe that the picture is due not only to the fact that there is an encephalopathy in Negroes but to other factors. When one studies severe encephalopathies one always finds some other pathologic condition, such as hypertension; moreover, persons with encephalopathy are more susceptible to infectious processes. Nevertheless, I think that one can speak of a syndrome here. It is not a disease entity but a syndrome in which there are organic and racial factors; that is as far as we wish to go. In his clear discussion, Dr. Keschner came to the same conclusions. If some one says that the disorder is only an interesting picture and does not mean anything to him, we agree. We also find it an interesting picture, and it means something to us.

DR. THOMAS K. DAVIS: The question has already been asked: Is this a psychic or an organic neurologic regression? I wish to suggest that one might secure information on this point if one exposed a patient with this disorder to stimulating rhythmic music. I predict that the patient would react to the psychic stimulation, that his motility would be markedly affected and that one would have partial proof that the motor disorder in this "motility psychosis" is of psychic origin. One must remember that the Negro is naturally a rhythmic "animal." I suggest that Dr. Wortis expose his next patient to music that is rhythmic and stimulating.

DR. HERMAN WORTIS: In reply to Dr. Davis: I doubt whether any regression is either psychogenic or organic—both factors must play a role. I think regression may be predominantly psychogenic or predominantly organic. Dr. Davis' suggestion might prove of value.

Dr. Keschner has agreed in substance with what we have said, and the objections which he raised have already been answered by Dr. Schilder. I might add that the incidence of syphilis in Negroes is, of course, high. We have never seen this disorder, however, in a syphilitic person.

Dr. Riley commented on the similarity of the movements in these cases to those observed in children. These moving pictures, however, were taken at random and in no way give a complete picture of the man's behavior.

ACUTE DISSEMINATING ENCEPHALOMYELITIS. DR. CHARLES DAVISON and DR. SAMUEL BROCK.

This paper was published in the December 1937 issue of the *Bulletin of the Neurological Institute of New York.*

DISCUSSION

DR. ARMANDO FERRARO: The 2 cases which Drs. Davison and Brock have so convincingly described constitute another example of the difficulties which both the clinician and the pathologist, but especially the clinician, find in labeling nervous complications in the course of certain infectious diseases. In the first case the process was described as degenerative, no inflammatory cells being present, and in the second, as typically inflammatory. Nevertheless, in both cases the condition was labeled encephalomyelitis.

Therefore, unless one is ready to disregard the concepts of inflammation and degeneration and agrees to use freely the term "encephalomyelitis," irrespective of the inflammatory nature of the pathologic process, the labeling of nervous complications in the course of or following infectious diseases should be limited at first to the general terminology of cerebral or cerebrospinal complications of this sort. Pathologic confirmation of the inflammatory or degenerative nature of the demyelinating process, if demyelination is present, would justify only later a more precise labeling of the process as encephalitis or encephalopathy with a subhead of acute or chronic demyelination, of patchy or diffuse type.

I am interested that Davison and Brock pointed out the identity of the pathologic lesions in their cases with those described in the course of other infectious conditions, such as measles and smallpox, or following vaccination. In a consideration of the pathogenesis of such encephalitides or encephalopathies, it seems to me that one cannot easily conceive of identical lesions resulting from the direct action on the nervous system of different viruses. It is more probable that the lesions result from the direct action on the nervous system of toxic substances liberated in the course of the systemic infection which precedes the nervous complication or from allergic phenomena due to absorption of toxic substances.

Such contentions are supported by the recent experiments of Rivers, who succeeded in reproducing in monkeys typical encephalomyelitis with demyelination by subcutaneous injections of a sterile aqueous or alcoholic extract of rabbit's brain. It is possible either that a myelolytic ferment is liberated by the injected material or that neurotoxins are generated in the monkey's organism and are responsible for the demyelination.

In order to investigate further this interesting question, my associates and I, at the New York Psychiatric Institute and Hospital, are repeating Rivers' experiments, with the view to going further and establishing the part of the alcoholic or aqueous extract which is responsible for the encephalomyelitis. We propose to do this by fractioning all the elements, proteins and lipoids, contained in the extract and investigating the result of their injection separately or in various combinations.

As for the similarities, or even the identity, of demyelinating processes following various infectious diseases—the so-called acute encephalomyelitides and the so-called acute multiple sclerosis—a resemblance accepted, if I am not mistaken, by Davison and Brock: It would take too long to discuss at present the pros and cons for their unification or separation.

To express briefly my views: I may say that I favor the effort at unification of all the primary demyelinating processes. It is possible that, even though various etiologic agents may be responsible for the systemic infection, toxemia or fundamental metabolic imbalance producing the demyelination, the demyelination itself may result in all cases from an identical basic mechanism, as yet unestablished. The variations in extension of the demyelination, in the acute and subacute course of the process and in the type of cellular reaction may be interdependent and also dependent on local factors as well as the pathologic constitutional make-up of the nervous system, which is an aspect of the general constitutional make-up of the individual patient.

DR. E. D. FRIEDMAN: Earlier, one would have called this condition acute multiple sclerosis. I think that most will agree with Dr. Ferraro that the tendency to unify all the virus infections of the nervous system is steadily gaining ground.

I shall confine myself to a simple discussion of the nosologic relationship between the syndrome which was presented and that of so-called influenza. I recall many years ago, when cases of fulminating epidemic encephalitis were first observed, that Schlesinger reported seeing in his wards in Vienna (at the time that von Economo was observing his cases of encephalitis lethargica) cases of epidemic influenza and of encephalitis at the same time; it was his notion that there was a nosologic relationship between the two. I also recall that soon after the epidemic came to America, I saw a case in which the disease ran a fulminating course. At postmortem examination there were observed in the lungs the characteristic lesion of pandemic influenza and, at the same time, in the nervous system the lesions which have come to be associated with virus infections of the central nervous system, namely, inflammatory reactions around the vessels, neuronophagia, loss of myelin and so forth. It seems, therefore, that there must be some relation between influenza and this neurologic entity, which all have been seeing for many years.

The exact etiologic agent responsible for influenza is not yet known. The work of Francis and others points in a certain direction; the ability to neutralize the virus of epidemic influenza by means of serum from convalescent patients seems to indicate specificity. But the last word has not been said on the subject, and it is not known whether the virus which produces pandemic influenza has anything to do with the clinical syndrome in the nervous system. It seems that, in theory, the soil for this filtrable virus is prepared by some other infection. On a previous occasion I said that there was a somewhat similar mechanism underlying the disappearance of the Pirquet reaction during measles. When the organism is warring with measles, the Pirquet reaction disappears because the whole immunologic mechanism is concerned with fighting the immediate infection; other infective organisms are not being attacked at the same time, so that there is the possibility of the lighting up of latent tuberculosis after measles or pertussis. Recently, Neal and Wilcox (*Science* **86**:267 [Sept. 17] 1937), of the Department of Health of New York City, reported 16 cases of neurologic illness following influenza, in none of which were they able (by the method of Francis and Magill) to obtain from the serum antibodies that completely neutralized the virus of influenza; they concluded that there is no definite proof that the virus of influenza

is capable of producing neurologic disturbances. They stated that the final word has not been said on the subject. It seems to me that the clinician's word should not be cast aside altogether. If he sees cases in which the disease resembles pandemic influenza and is followed by neurologic disturbances, the assumption, I think, is fair that the two are in some way related.

DR. FOSTER KENNEDY: I cannot help but comment on what Dr. Friedman has said. I wish to report a conversation I once had with Dr. Charles Dana. He told me that in 1882 there was a severe epidemic of influenza in New York, in the course of which physicians saw conditions called "grippal catalepsy" in which the patients became catatonic and were covered with sweat. As far as I know, I am using his words. Many of the patients died, and in the brain and cord lesions were observed similar to those that one is accustomed to see in multiple sclerosis, a disease which at that time was in the forefront of the neurologic mind. Such was the sequence of events, as observed by a good clinician: influenza, "grippal catalepsy" and multiple sclerosis.

DR. I. S. WECHSLER: May I say that this excellent paper fills one with a certain amount of despair of one's ability to resolve the question in pathologic terms? It seems to me that a blind alley has been reached in this investigation, as it has in other pathologic problems. The theoretical attempt either to unify or to diversify can lead to no explanation. It is an effort to substitute one unknowable for another. I do not think that this problem will be solved either by the clinician or by the pathologist; ultimately it is for the biochemist, the serologist and the bacteriologist to answer. One is dealing with a fundamental reaction of the nervous system to noxious agents the nature and specific action of which are not known. The encephalitis or the encephalomyelitis is not as important as the structure and the specific reactivity of the nervous system itself. One sees various noxious agents bringing about the same pathologic change and the same agents causing varied pathologic reactions. Surely, the answer to this problem cannot be supplied by the clinician; I doubt whether it can be given by the pathologist, because he generally deals with end-processes. The whole clinical discussion on acute encephalomyelitis and multiple sclerosis is, it seems to me, only going around in circles—circles which have been traversed for many years. With all due respect to the pathologist, I do not think that the answer is along morphologic lines alone.

DR. CHARLES DAVISON: I have nothing to add to the discussions, except to say that I agree with most of the points brought out. I agree with Dr. Wechsler's remark that the pathologist cannot give the final answer to this question, but I do not think that the chemist or the serologist alone will do so. No single investigator will. Cooperation of the clinician, the pathologist, the biochemist, the serologist and others will be necessary for complete understanding of the various types of encephalomyelitis and encephalomyelopathy.

LOCALIZED NONSUPPURATIVE ENCEPHALITIS RESULTING FROM ADJACENT INFECTION IN THE SKULL. DR. E. MILES ATKINSON (by invitation).

Borries, of Copenhagen (Otogene Encephalitis, *Ztschr. f. d ges. Neurol. u. Psychiat.* **70**:93, 1921), drew attention to a condition which, following suppuration in the ear, presented the signs of an abscess of the temporal lobe but yielded negative results on exploratory puncture, and from which, nevertheless, the patient recovered. He called this the "syndrome of abscess without abscess" and suggested hemorrhagic encephalitis as the cause. Adson (Pseudo-Brain Abscess, *S. Clin. North America* **4**:503, 1924) reported 3 similar cases, while Symonds (Some Points in the Diagnosis and Localisation of Brain Abscess, *J. Laryng. & Otol.* **42**:440, 1927) reported 3 more. A few other scattered cases have been recorded, but the condition has not received wide acceptance. I believe that it is more frequent than would appear from the meager literature but often goes unrecognized, that it is of practical importance that the concept of brain infection

from a focus in the skull should be enlarged to include this condition and that there are certain points in the symptomatology which render possible diagnosis without exploratory puncture.

Material.—The conclusions given here are based on a study of 8 cases in my personal practice, 2 others in the recent experience of my colleagues, Dr. Marvin Jones and Dr. A. S. Wilson, of the Manhattan Eye, Ear and Throat Hospital, to whose records I have been given access, and also cases in the literature, some of which, unfortunately, were not adequately recorded. In all cases described up to the present the abscess has been secondary to disease of the ear, and in all it has been in the temporal lobe, except the 1 instance of cerebellar abscess. In 9 of the 10 cases reported in this paper, the abscess was in the temporal lobe, and in 1, in the frontal lobe consequent to frontal sinusitis.

Pathologic Picture.—This must be largely conjectural since most patients recover; the few cases reported in the literature in which the outcome was fatal have not been completely studied. I have had opportunity to investigate the material in only 1 case microscopically.

There are two main groups, a serous and an infective encephalitis. 1. Adjacent Serous Encephalitis (3 cases): As a result of adjacent suppuration involving the dura, local cerebral edema is produced similar to the aseptic meningitis which occurs under the same circumstances, the *méningite de voisinage* of the French writers. The process is an *encéphalite de voisinage*. Such an encephalitis in minor degree is presumably present in many instances and is the cause of the frequent localized headache, but only when it involves the brain substance to some depth does it give rise to true localizing signs. The condition is associated with either pathologic exposure of the dura or an extradural abscess. It is heralded by a convulsion, which may be repeated at intervals until drainage is established, shows residual signs between convulsions and usually disappears rapidly, completely and permanently as soon as the cause has been removed; all this supports the supposition of simple edema. However, if drainage is delayed too long the process may pass into the form described in the next group.

2. Adjacent Infective Encephalitis: Here the adjacent infection has done more than cause edema; it has invaded the brain substance and produced localized encephalitis. The ultimate result of this invasion will depend on the nature and virulence of the organism concerned. (*a*) Suppuration. This is the usual sequel—the area of encephalitis breaks down to form an abscess. With this aspect my only concern now is the question of differential diagnosis. Has or has not suppuration taken place?

(*b*) Nonsuppuration. Again, progression may be in one of two directions: (1) The inflammatory process may subside and the patient recover (3 cases). This group includes the cases described by Borries under the head of "abscess without abscess" and nearly all the reported cases, including those of Adson and Symonds. On the basis of the next subgroup, one assumes the presence of an area of encephalitis of limited, but sometimes considerable, extent which gradually resolves. It may progress to the point of producing complete hemiplegia and aphasia, and yet the patient may recover.

(2) The inflammatory process may spread and cause the death of the patient by the intensity of the infection and the accompanying increase of pressure or by involving and even breaking through the wall of the ventricle and causing meningitis (4 cases). An area of hemorrhagic infiltration, indefinitely demarcated, is observed, sometimes containing patches of necrosis, which demonstrate the intensity of the infection. It is a lesion of the latter type which is often called, wrongly, an "acute brain abscess."

Differential Diagnosis.—The difficulty is in deciding between encephalitis and abscess. Symonds (Some Points in the Diagnosis and Localisation of Brain Abscess, *J. Laryng. & Otol.* **42**:440, 1927) said that this localized encephalitis presents no characteristic clinical picture, while Borries (Encéphalite otogène

hémorragique, *Rev. de laryng.* **53**:49, 1932) held that the only way to decide is by exploration. Admittedly, differentiation may be difficult, sometimes impossible, but I believe that it can usually be achieved and that it is important from the point of view of treatment. In the accompanying tabulation are listed points in differentiation of the two conditions.

	Encephalitis	Abscess
Onset	Abrupt, often with convulsions	Gradual
Localizing signs	Widespread from the start	Localized and slowly progressive
Mental state	Restlessness; irritability; delirium	Drowsiness, increasing to stupor
Course	Variable and rapid	Steadily progressive
Temperature and pulse rate	Raised to 101 F. or more; associated	Normal or subnormal; low, dissociated
Papilledema	Early and usual	Late and often absent
Spinal fluid	Pressure high; cells many, 100 or more, polymorphonuclears or lymphocytes	Pressure moderate; cells few; mainly mononuclears
Dissociation syndrome	Absent	Present

Treatment.—When the diagnosis is certain, operative measures should be limited to decompression with, other things being equal, incision of the dura. Exploration, with its risk of converting localized into spreading encephalitis, is to be avoided unless essential to diagnosis.

Summary.—The points of practical importance are: 1. Suppuration in the skull, especially the ear, may cause localized encephalitis, which can be diagnosed from the clinical picture.

2. In a patient with signs of encephalitis and a suppurating ear, the encephalitis may be due to the condition in the ear and need not be a clinical entity.

3. Encephalitis must be differentiated from abscess, to avoid the danger of unnecessary exploration.

4. Negative results from puncture for a supposed abscess does not necessarily mean that the abscess has been missed or demand further exploration.

DISCUSSION

DR. FOSTER KENNEDY: This subject is of extraordinarily pregnant interest when one is confronted with a patient and it is necessary to say yes or no in regard to operation. I was baffled by Dr. Atkinson's inclusion of cases of what he described as "pyogenic encephalitis." I thought that the title of the paper was "nonsuppurative encephalitis." I presume that "pyogenic" means "pus forming" and that "suppurative" means that pus has formed; so I am not sure that there is not here some contradiction in terms.

I have also been interested in a type of encephalitis in which there is infection of the ear and a sudden cerebral syndrome is imposed on this infection—with focal signs of destruction of cerebral function but no abscess. To explain my point, I shall report a case briefly. More than ten years ago I was called to the Rockefeller Hospital to see a boy aged 8 who had become hemiplegic. He had subacute otitis media on the left side, but he was in the hospital not for this condition but for nephritis. He had, I judge from the history of nephritis, a poor water balance. The nurse stated that he had been well at 7:30 a. m., when she gave him breakfast. At 8:30 she spoke to him, and he did not answer; he seemed drowsy. He could be aroused but could not speak. He was not able to move his right arm and leg. I saw him within forty minutes after the onset, at about 9 a. m., at which time he was paralyzed in the right arm and leg; there was a Babinski sign on the right, he was totally aphasic, exhibited total hemianopia and did not seem

to feel well on his right side; however, as he was aphasic I could not be certain of this. The ocular fundi were normal. He was irritable and had a stiff neck. The speed of onset and the fact that he had nephritis and otitis media of a subacute type led me to make a tentative diagnosis (out of pure ignorance) of acute edema of the left side of the brain on a toxic, but nonbacterial, basis. I was not prepared for the fact that the boy seemed well at 7 o'clock that night. Exactly what happened to him I do not know. A lumbar puncture revealed about 80 cells; so his condition came into the category of Dr. Atkinson's serous encephalitis. As many with me at the Bellevue Hospital know, I am rather "hipped" on the subject of localized edema of the brain. I believed then that there was localized edema of the left temporal and parietal lobes, induced by the inability to balance fluid, largely by reason of the nephritic situation, and the contiguous toxicity of the otitis media. This, however, is a different thing from the entrance of bacteria into the brain. Pyogenic encephalitis is simply, as far as I can see, an abscess which has not formed a wall and perhaps has not formed pus. After all, streptococcic infection of the foot is a malignant and grave situation, fatal perhaps, but there is no pus. That there is no pus does not mean that it is benign; so there may be a certain confusion in putting the two things together. I think that osteomyelitis of the skull, otitis media and suppuration of the scalp are all capable of producing alterations in the fluid content of cerebral tissue without bacterial invasion. If the fluid content of the cerebral tissue is sufficiently interfered with function is abrogated by reason of the fluid, but if it is not interfered with too severely function remains. That is a different pathologic process from infection of the brain with a pyogenic organism and the breaking down of nerve tissue by bacterial action, which causes necrosis of tissue and irreparable damage. The patients do not always recover; some die. The reason that some persons with this condition are operated on and no abscess is disclosed may be found by comparing the situation to a streptococcic infection of the foot. If one is foolish enough to invade the foot in a case of streptococcic suppuration, one finds that there is nothing to drain. The condition in the brain is simply a bacterial and serous amalgam, as it were. It is on the whole very malignant. However, the truly serous conditions are benign; it is important to understand this when one sees this form of encephalitis, so as not to advise invasion by operation. It can be, as Dr. Atkinson pointed out, differentiated from other conditions by the rapid onset, the high cell count of the spinal fluid, the irritability and the variable rather than progressive course. At best, however, one has to rely on the *imponderabilia* of one's senses.

Dr. Isidore Friesner (by invitation): Some otologists who have lived for many years have seen a few of these cases. No one has seen many. As a fact, the reports in the literature are usually of one, two or three cases. If any one was as stupid as I in the first case which I saw, in which I made exploration and was able to congratulate myself on the patient's recovery, in spite of everything I did, he, like me, will be glad to forget such cases. The girl, who was a youngster at the time, had scarlet fever and mastoiditis on the right side, together with adequate physical signs and symptoms, according to the neurologist and the neurosurgeon, to indicate thorough exploration of the right temporal lobe. I have often wondered about this patient, and I am glad to have heard in the passing years that she recovered, grew up, married and had several children.

Dr. Kennedy's discussion is extremely interesting, but I wish to call attention to a point with regard to the bearing that Dr. Kennedy's discussion has on Dr. Atkinson's presentation. It would be unusual if, through such remote causes as disturbance in the water balance, nephritis or inflammation in the scalp, one should have phenomena such as Dr. Atkinson described. I believe that he did not stress sufficiently that the phenomena apparently occur always as a sequel to lesions in the adjacent portion of the brain—the portion adjacent to the ear.

It is extremely interesting and timely that an attempt should be made to classify these conditions, although I must agree with Dr. Kennedy that there is confusion in regard to the so-called hemorrhagic infections of the brain. It must

not be forgotten that in the bony focus immediately adjacent to the dura are pathogenic organisms; in over 90 per cent of cases these are hemolyzing streptococci.

The question of the action between the tissues and the infection involves the entire mechanism of immunity, which is too broad to be discussed here; yet this may explain why in one case there is suppurative encephalitis and in another hemorrhagic encephalitis. It is a question not only of the specific organism but of the individual host's reaction to the specific organism.

Dr. Atkinson states frankly and justly, under the caption of the pathologic picture, that this is bound to be conjectural in cases of nonfatal outcome. He postulated two main groups, a serous and an infective encephalitis. Now, to me, the situation with regard to *encéphalite de voisinage* is not markedly different from that which obtains in *méningite de voisinage*, and although meningitis is, strictly, not the subject under discussion, it is nevertheless closely allied to it. One is asked to believe that in meningitis an infection in the adjacent bone involves, but does not penetrate, the dura. Surely, the presence of micro-organisms in the spinal fluid is not an adequate and the sole criterion for the diagnosis, first, because there have been many instances of fatal meningitis in which at no time during life could organisms be demonstrated by smear or culture in the spinal fluid and, second, because there are instances of brain abscess in which streptococci were reported in the spinal fluid but there was no meningitis.

Is one supposed to believe that micro-organisms in an acute focus in the bone adjacent to the dura are marshaled and attack the dura, but that at the crack of a whip or the blast of a whistle they "about face" and retreat, without a single organism penetrating this structure? Repeated attacks are supposed to occur until, finally, the organisms penetrate. This theory does not appeal to me as rational, and I believe that there is no difference in essence between *méningite* or *encéphalite de voisinage* and the infectious type. The difference is one of degree. Is there not in the action of sulfanilamide collateral evidence? Sulfanilamide is not bactericidal. Its use arouses, or probably enhances, some protective mechanism in the body tissues. It is this protective mechanism that overcomes the minimal infection, whether it is in the meninges or in the brain. The concept of meningeal reaction or encephalitis resulting simply from contact without infection is, I believe, erroneous.

It seems to me that a great service is rendered by Dr. Atkinson's presentation. This does not lie in the accurate differentiation between what might be called encephalitis capable of resolution and encephalitis with abscess formation. I am sure he will agree that this differentiation is still somewhat problematic. However, the good that emanates from this work is the obvious, though unexpressed, urge toward greater conservatism on the part of cranial surgeons, in regard to the problem not so much of whether to operate but of when to operate.

Dr. E. D. Friedman: Dr. Kennedy and Dr. Friesner have already indicated that these are cases which all encounter on occasion; one is in a quandary as to whether there is a brain abscess or not. There are many references in the literature to "pseudo-abscess," and one must agree with Dr. Friesner in his interpretation of the various types of encephalitis. The virulence of the organism and the reaction of the host to this organism determine the clinical picture in the individual case. In one instance the pathologic process will be a serous inflammation; in another it will be an infective process of greater virulence, and in the most virulent forms there is true abscess formation. My colleagues and I recently had an interesting experience at the Beth Israel Hospital. The patient apparently suffered from mastoiditis of long standing, and signs pointed to a focus in the temporal lobe. The diagnosis was not easy. There was no history of acute otitis, and we all thought the lesion in the brain was neoplastic. There were considerable papilledema, hyperreflexia on the left side and a lesion of the third nerve on the right (indication of pressure against the crus); we operated, expecting to see a tumor of the brain, but instead saw a hemorrhagic area of softening in the tem-

poral lobe; the patient made a complete recovery. I suppose that this favorable outcome was due to the fact that we waited so long before operating.

I believe also that there is some relationship between this syndrome and that which Symonds has described as otitic hydrocephalus and which others have designated as toxic hydrocephalus. It is important that the neurologist and the otolaryngologist recognize these intracranial complications secondary to disease of the ear or sinuses, which are not suppurative.

Dr. S. Bernard Wortis: Did Dr. Atkinson have the opportunity to culture the brain tissue in the cases of hemorrhagic encephalitis to determine the presence of organisms? My experience and that of my colleagues at the Bellevue Hospital with respect to abscess of the brain seem to throw doubt on one item in the chart which Dr. Atkinson has shown, namely, that the state of consciousness which exists in the presence of brain abscess is not necessarily progressive coma but one in which the patient passes into and out of stupor during a period of several days. We have thought that such a reaction is a characteristic sign of abscess of the brain.

Dr. E. Miles Atkinson: Dr. Kennedy queried my use of the term "pyogenic" to describe a variety of nonsuppurative encephalitis, and I agree with him that it is confusing. However, I was in difficulty as to how to describe briefly the process in these cases. My idea in calling it pyogenic was that the infection was due to a pyogenic organism, though it did not necessarily form pus. It may go on to form pus; it may be a stage on the way to abscess formation, but, with Dr. Friesner, who said in different words what I tried to express, I look on the question as one of a balance between the virulence of the organism, on the one hand, and the resistance of the patient on the other. A varying degree of virulence in the organism will produce a varying type of inflammation. A relatively avirulent pathogenic organism will produce an area of inflammation which does not go on to pus formation, whereas the reaction to a virulent pathogenic organism may progress to form pus. On the other hand, it may not. The streptococcus is a pyogenic organism, but it does not always form pus. A streptococcic infection of the finger often does not. The particular, virulent type of infection that physicians are liable to acquire in postmortem work does not produce pus. "Pyogenic," therefore, may have been an unfortunate term, and if Dr. Kennedy will help me out of my quandary by suggesting a better word to express what I was trying to say I shall be pleased to adopt it.

Dr. Friesner pointed out that I had not stressed enough the fact that the area of encephalitis is always adjacent to the focus of infection in the skull. I thought that scarcely necessary, as the title of the paper was "Encephalitis Resulting from Adjacent Infection in the Skull."

In answer to Dr. Wortis' first question: There were no cultures of the brain tissue. I said I was afraid that the pathologic study was sadly deficient. In answer to his second question with regard to the passing into and out of coma in the case of brain abscess: I do not think this happens until the abscess is fairly well advanced or unless it is acute, when it is, I maintain, really encephalitis. Is not the passing into and out of coma due to the varying amount of encephalitis surrounding the abscess? This is a condition which always applies unless the abscess is of such chronic nature that it simulates a tumor, with the capsule so thick that there can be no encephalitis around it.

Book Reviews

Autonomic Neuro-Effector Systems. By Walter B. Cannon and Arturo Rosenblueth. Price, $4. Pp. 229, with 42 illustrations. New York: The Macmillan Company, 1937.

The book deals with a part of modern physiologic research in which progress made during the past sixteen years is conspicuous. In 1921 Otto Loewi reported his classic experiments, in which he showed for the frog's heart that stimulation of autonomic nerve fibers leads to liberation of definite chemical substances which influence the effector organs. Later, Dale, Feldberg, Cannon, Rosenblueth and many others not only proved the validity of this concept of chemical mediators of nerve action for the autonomic nerves of cold-blooded and warm-blooded animals but showed that acetylcholine is liberated at the neuromuscular junction of somatic nerve fibers and at the synapse in the superior cervical ganglion. The paradox that sweat glands are innervated by sympathetic fibers but react strongly to parasympathetic drugs was better understood when it was found that the sympathetic sweat fibers are "cholinergic" rather than "adrenergic." As to the nature of the adrenergic substance, opinion is divided. Cannon and Rosenblueth still expound the theory that the adrenergic substance which they call "sympathin" is chemically different from epinephrine and consists of two substances responsible for the excitatory and the inhibitory effect which may be observed after stimulation of sympathetic fibers. That acetylcholine and sympathin are liberated under strictly physiologic conditions is shown by the fact that they appear in measurable quantities even under the conditions of reflex stimulation.

The significance of experimental results is best tested by the applicability of the concepts derived from such research and by the simplification of theoretical concepts, in spite of increased knowledge.

The investigations stand both tests well. The hypothesis that central excitatory and inhibitory states may be based on the formation of labile chemical substances has obtained a sound basis through these studies. The puzzling paradoxes, such as the Vulpian-Sherrington phenomenon and the paradoxical pupillary reaction, are now understood on the basis of a simple principle: By denervation the structure becomes more sensitive to its physiologic chemical mediator. Although the importance of the chemical mediators is shown with regard mainly to the peripheral effectors and not to the central nervous system, the book may be highly recommended to the neurologist who wants more information in this important field.

Correction of Speech Defects of Early Childhood. By S. D. Robbins, M.A., and R. S. Robbins. Price, $1. Pp. 65. Boston: The Expression Company, 1937.

Mr. and Mrs. Robbins have written a useful little book, with many good suggestions about the treatment for speech defects. Forty-five pages are given over to words in lists and pairs and to sentences and short passages which bring out difficulties and help to correct special speech troubles. Brief descriptions and short directions for treatment are given for delayed speech, ideolalia, cluttering, nasal speech, dialects, stuttering and lisping. Most emphasis is placed on the two disturbances last mentioned.

For treatment of stuttering, the following directions are given: The stutterer should be taught (1) to sigh; (2) to vocalize the same sigh; (3) to "loud-sigh" all conventional vowels and words of one syllable; (4) to practice mouth play without tension and to combine this with the loud sigh; (5) to combine the pairs of vowels and to read vowel sentences in a low-pitched monotone, with stress on the accented vowels; (6) to read poetry, with stress on the accented vowels, and

ordinary prose in like manner; (7) to close the lips the instant he begins to stutter, before struggling and to sigh if that is necessary to relax, and (8) in order to avoid stopping in the middle of a sentence, to pretend that he omits a hard consonant and make the vowel which follows it longer than usual.

If a child has not become conscious of the fact that he stutters, his attention should not be called to the trouble by correcting his speech, lest this confirm the stuttering. Instead of using the directions outlined, one should always speak to the child in the manner described. Many children who have just begun to stutter have overcome the defect in a few months by unconsciously imitating the manner of speech used by their parents.

"Nervous tension" is mentioned as a cause of stammering, but nothing is said about the psychologic aspects. This is a distinct defect in the book, for much can be done in cooperation with the parents to relieve tension without working directly with the child. As a guide for treatment the book is useful after the teacher has seen the method demonstrated, but is much less useful without such demonstration.

Erbgesundheitsgesetz und Ermittlung kindlicher Schwachsinnszustände mit den Entwicklungstests von "Bühler-Hetzer." By Dr. Med. E. Vowinckel. Price, 3.40 marks. Pp. 54, with 28 illustrations. Stuttgart, Germany: Ferdinand Enke, 1936.

A procedure of sterilization in the interests of race betterment soon becomes involved with measurements of mental capacity. The present monograph is concerned with recent German efforts of this nature. It consists principally of twenty-eight case reports illustrating, in an elementary way, application of the Bühler-Hetzer procedure to the function. Vowinckel appears to have acquired this technic primarily *ad hoc,* and to have only limited perspective on related endeavors; foreign work is practically ignored, though there are mentions of Terman and Gesell.

It is from the cultural standpoint that the work has its chief interest to the American profession. Several years ago it was well said that American psychology was strong in method but weak in theory, and German psychology strong in theory but weak in method. This study bears out the statement and makes a further suggestion. Its basic criticism of the Binet procedures is well founded, and there are qualitative insights that in this country would be looked for only in a much more seasoned worker in the field than the author appears to be. However, with these disparities in theory and method, there seems to have been in Europe the greater readiness to attempt social application of advancing psychologic knowledge. Such experimentation as the *Erbgesundheitsgesetz* is, naturally, easier in a totalitarian state, though the general process has not been a function of totalitarianism. The ideology underlying the present study appears in such passages as the following: "Es wurde dabei oft nicht genügend bedacht, dass es moralische Versager ohne intellektuelle Minderleistungen kaum geben kann (Dubitscher)" and, with regard to a case in which a developmental quotient of 61 was associated with an inferior family history, "Man wird in diesem Fall möglichst geringe Mittel zur weiteren Pflege des Kindes anwenden" (pp. 9, 43). The economic stringency under which the nation operates doubtless plays a part in such an expression of diminished concern for the defective person.

The implication (p. 53) is that in the cases concerned sterilization is permissive at the age of 10 years and mandatory by the fourteenth year. At these ages psychometric technics will long have passed the point of diminishing returns for the understanding of such children. Besides the suggestions on qualitative observations, the author lays more stress than is usual in America on matters of rapport, especially as to physical surroundings. Clinic facilities are, in general, far from satisfactory, and the preferred procedure is to go into the homes (*Spieltante*), where the children will be in accustomed surroundings and the elders will not be waiting impatiently. This has not appeared so advantageous in this country, where the clients have perhaps better furnished and less "domestic" homes.

Die Nebenschilddrüsen-Epilepsie. By Kurt Hoesch. Price, 23.80 Swiss francs Pp. 135. Berlin: S. Karger, 1937.

The diagnosis of parathyroid epilepsy is based on the following signs: (1) mechanical and electrical overexcitability of peripheral nerves; (2) initial tetany and cataract as shown by slit lamp examination; (3) hypocalcemia; (4) typical signs of parathyroid insufficiency, such as trophic disturbances in the nails, teeth, hair and skin; (5) increase in the Q-T interval of the electrocardiogram, which depends on the hypocalcemia and is reversible on administration of calcium and solution of parathyroid, and (6) effect of organotherapy. While genuine epilepsy produces symmetrical convulsions, parathyroid epilepsy may produce unilateral convulsions as well.

Parathyroid epilepsy may appear as early as in the first month of pregnancy, but the fourth and fifth months are particularly dangerous. Hormone therapy is necessary in these cases and makes interruption of the pregnancy or sterilization unnecessary. The dose of solution of parathyroid necessary in the treatment of parathyroid epilepsy varies for different persons. It should be determined by repeated calculations of the blood calcium as controls. This therapy is effective in all cases of initial parathyroid epilepsy, but not after irreversible changes develop in the brain. It is without success in treatment of so-called genuine epilepsy.

The monograph will be valuable to those interested in parathyroid epilepsy.

Alcohol—One Man's Meat. By E. A. Strecker, M.D., and Francis J. Chambers Jr. Price, $2.50. Pp. 230. New York: The Macmillan Company, 1938.

This book presents a splendid discussion of the alcoholic neurosis from the standpoint both of its psychologic background and of its rational treatment. It emphasizes a fact which needs constant reiteration if the alcohol addict is to be given the same chance for treatment as other neurotic persons, namely, that the fundamental neurosis is a desire to escape from reality and its consequences. While this appears to be obvious, it is too frequently lost sight of, with the result that the alcohol addict is regarded as hopelessly beyond any but custodial treatment. The authors point out that 90 per cent of alcoholic persons are introverts who drink to become more socialized and, hence, more extroverted. Often the reason for drinking lies in a profound sense of inferiority, which can be overcome only by recourse to alcohol, an act which is the beginning of a vicious cycle: drinking to escape and escape through drinking. The section on the psychologic makeup of the alcohol addict is well constructed and shows an excellent understanding of the man and his problems. It is full of sound, common-sense reasoning, which makes the needs of the alcohol addict all the clearer by stripping him of all but his fundamental neurosis. It contains a searching analysis of the personality of the alcoholic patient.

Most hopeful of all is the contention "that a well-organized psychotherapy, which is not strictly psychoanalytical, is a fundamental requisite in the successful treatment of alcoholism." This is in itself a real advance and a gratifying attitude, for it assumes that the alcohol addict can be treated, that under the proper circumstances he can be cured and that custodial care, far from being the ideal treatment for chronic alcoholism, is merely temporizing until a more fundamental approach is possible. The second half of the book is devoted to treatment of the alcoholic neurosis. The method employed successfully by the authors cannot be given in detail here. Briefly, it consists first and foremost of encouraging a real desire on the part of the patient to get well, to recognize that alcohol is for him a drug that he must never touch and to proceed with this fundamental axiom to reeducation through psychotherapy and whatever physical therapy is essential.

The book is a sound, sane and extremely readable discussion of the problem of the alcohol addict, who may truthfully be regarded as the neglected man. It is hopeful in its approach and sound in its treatment. It can be recommended to all physicians, regardless of their special field of practice.

Pathology of the Central Nervous System: A Study Based upon a Survey of Lesions Found in a Series of Fifteen Thousand Autopsies. By Cyril B. Courville, M.D. Price, $5.75. Pp. 344, with 200 illustrations. Mountain View, Calif.: Pacific Press Publishing Association, 1937.

This volume presents thoroughly practical work on neuropathology, as good as any that has appeared in the English language. It is simple and fairly complete, emphasizing the common disturbances in the nervous system and correlating these deviations with the clinical features, on the one hand, and pathogenesis, on the other. The fine work that the author has done on craniocerebral injuries is summarized in 60 pages, with many illustrations and diagrams, and forms by far the finest part of the book. The discussion of the pathways of infection of the nervous system and the mechanism of abscess formation is also effectively treated, but the chapter on syphilis is not well done. Particularly interesting is the study on the incidence of the various neurologic disorders, based on a series of 15,000 autopsies performed at the Los Angeles County Hospital. The book contains many gross photographs and little of the tedious minutiae of microscopic description. The author may be accused of meticulousness in discussing the anomalies and malformations of the nervous system, but his breadth of view will be appreciated in the chapter on diseases of unknown etiology. In the clinicopathologic aphorisms, an appendix to the book, will be found sound judgment, good reasoning and expert pathologic knowledge that comes only with years of close contact between the clinic and the laboratory. The book is recommended to students because of its clarity, and to all physicians for its classic discussion of injuries to the brain.

Neurology. By Roy R. Grinker. Second edition. Price, $8.50. Pp. 999, with 406 illustrations. Springfield, Ill.: Charles C. Thomas, Publisher, 1937.

One admires the versatility and wide reading that the author shows in the first edition of this book and in bringing the material up to date in the second. The reading and abstracting, however, have left their imprint on the style; one feels that the book is a patchwork, not sufficiently knit together by a mature point of view. This is, of course, an advantage in some ways, for the opinions of various investigators are brought forward, but often without constructive comment. A shorter book with fewer quotations from various authors would be more convincing. A longer book would be more authoritative. The book falls between the two. The discussions of treatment, however, are concise and sound and express personal opinions evidently backed by experience and common sense.

In the second edition new material has been added and much revision made in chapter 11, on the vegetative nervous system. Such recent advances as electroencephalography are discussed in relation both to the physiologic activity of the cortex and to clinical application, as in the study of epilepsy. Tracings are shown from original workers which refute the text, for the waves in the grand mal seizure are fast, not slow, as Grinker states; also, the author uses the ambiguous term "psychomotor attack" to denote what Lennox calls the "psychic variant" and "automatism." Why not the time-honored, but sound, word "fugue"?

The chapter on the cerebral cortex is broadly inclusive; the theories of Head, Herrick, Lashley and Goldstein are epitomized, and a good description of Fulton's recent work on the frontal lobe follows. Chapter 20, on inflammatory diseases of the nervous system, describes in fifty pages the bacterial invasions of the brain, especially infections and abscesses. The next chapter of nearly fifty pages discusses encephalitis and virus infections in a thorough manner, up to the St. Louis epidemic of 1933. The new material on neuritis mentions, but does not emphasize, the recent discoveries concerning vitamin deficiency.

The book is well written, but there are many minor mistakes in references, spelling and the use of words. It strikes the reviewer as more a tour de force than a labor of love.